ROLE OF HUMAN IMMUNOGLOBULINS IN TETANUS

THESIS

FOR

MASTER OF SURGERY

(GENERAL SURGERY)

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SHANTI SWAROOP

C E R T I F I C A T E

This is to certify that the work entitled "ROLE OF HUMAN IMMUNOGLOBULINS IN TETANUS" has been carried out by DR. SHANTI SWAROOP himself in this department.

He has put in the necessary stay in the department as required by the regulations of Bundelkhand University.

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This is to certify that the work entitled "ROLE OF HUMAN IMMUNOGLOBULINS IN TETANUS", which is being submitted as thesis for M.S.(General Surgery) examination, 1990 of Bundelkhand University by DR. SHANTI SWAROOP, has been carried out under my guidance and supervision. His observations and results have been checked by me from time to time.

This work fulfills the basic ordinances governing the submission of thesis laid down by Bundelkhand University.

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Dated: 13-9-89.

(Shanti Swaroop)

C O N T E N T S

INTRODUCTION

INTRODUCTION

Tetanus is an infectious disease caused by clostridium tetani which is a grem positive, spore bearing obligatory anerobic bacillus. The word tetanus is an adaptative of the greek word 'tetanos' which is derived from the verb 'teino' which means 'to stretch'. Tetanus was first described by Hippocrates in the year 460 BC. The disease has a global prevalence and has high mortality. In rural India tetanus is among the first five leading causes of death.

The bacillus clostridium tetani was isolated by Nicolaier in 1884 and its exotoxin was identified by Kitasato in 1890. It is widely distributed in the soil and intestines of man and animals. It produces two distinct toxins - a haemolysin (Tetanolysin) and a powerful neurotoxin (Tetanospasmin). A third toxin - a non spasmogenic peripherally active neurotoxin has been identified, the role of which is not yet clear.

Tetanospasmin is an oxygen stable toxin responsible for the clinical manifestations of tetanus and is specifically neutralized by the antitoxin. It is produced locally and is absorbed by the motor nerve endings, and transported to the central nervous system along the peripheral nerves. The toxin is specifically fixed by the gangliosides of the gray matter, it acts

presynaptically and blocks the synaptic inhibition in the spinal cord. The abolition of spinal inhibition causes uncontrolled distribution of impulses initiated anywhere in the body. This results in muscular rigidity and spasm due to the simultaneous contraction of agonists and antagonists in the absence of reciprocal inhibition.

Destruction and necrosis of tissues, lack of adequate drainage, contamination with soil and infection with other bacteria, all favour the growth of spores. The incubation period of disease varies from 2 days to years. The interval between the first symptom of disease, usually trismus, and the onset of spasm is of great prognostic value (period of onset).

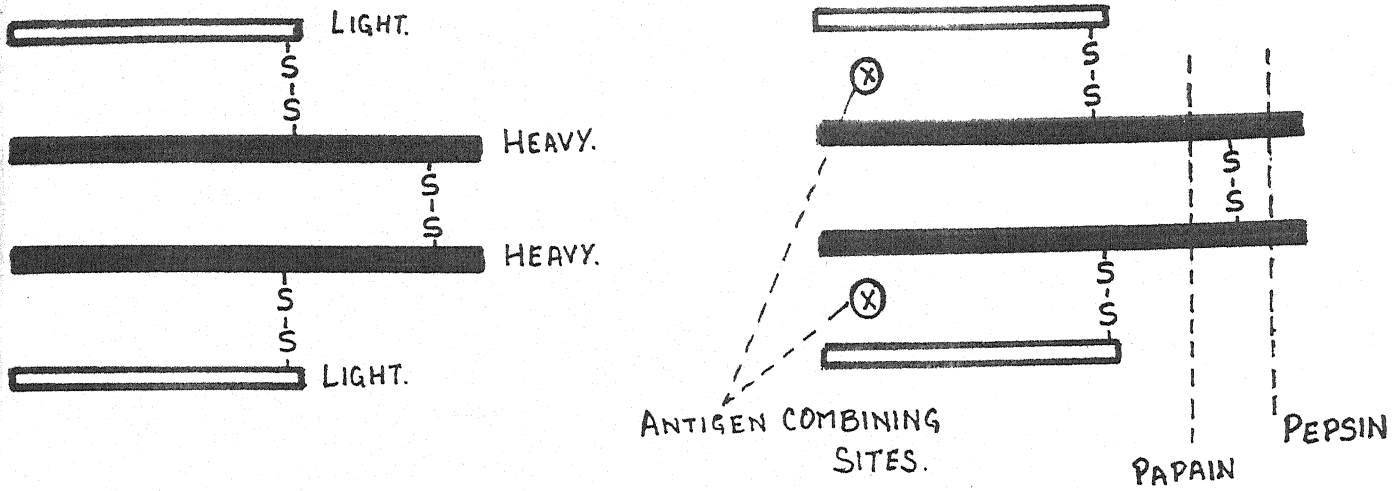
Tetanus may manifest at any age and may be divided into neonatal tetanus, childhood tetanus and adult tetanus. Out of these neonatal tetanus has the highest contribution to mortality. Geographical, social cultural and economic factors interrelate to form an important back ground for the prevalence of this disease. Illiteracy, inadequate medical care, unhygenic obstetrical practices, lack of immunization and ignorance all contribute to the high incidence and mortality of this disease.

The annual mortality from tetanus all over the world is about 50,000 (Bianchi, 1961) Bytchenko,

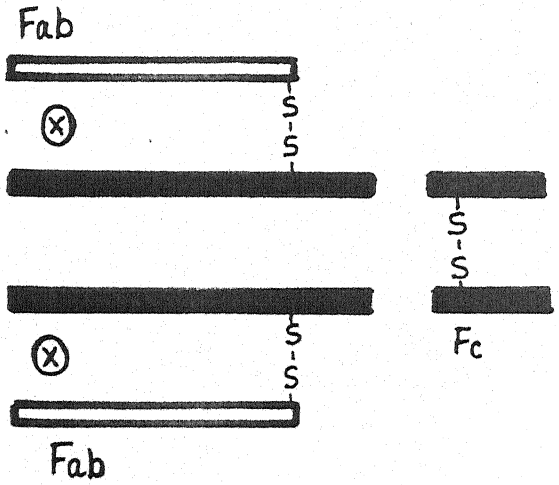
1966). However, the disease is more common in tropical countries and developing nations. Tetanus is more common in places with a warm and moist climate. Over 50,000 cases are reported annually in India by health authorities. Basu et al (1984) reported the prevalence of tetanus Neonatorum all over the 14 states and Union territories of India. The highest mortality due to tetanus was found in Uttar Pradesh.

Tetanus is a preventable disease. It is produced by the action of toxin, hence the most important method of prevention is to build up the immunity by active immunization. For active immunization, tetanus toxoid is used. Passive immunization can be done by antitetanus serum of equine origin but it carries the risk of hypersensitivity. Passive immunization without the risk of hypersensitivity can be done by human anti-tetanus globulin (ATG) which is effective in smaller doses with longer half life (3-5 weeks). At present intramuscular human antitetanus globulins are being used. Intrathecal use of human ATG by some workers shows good results.

The antitetanus immunoglobulins when given systemically, these large molecules cannot cross the blood brain barrier and so cannot neutralise unfixed toxins already present in the CNS while intrathecal administration establishes a direct contact. Now-a-days



STRUCTURE OF IMMUNOGLOBULIN, MOLECULE.



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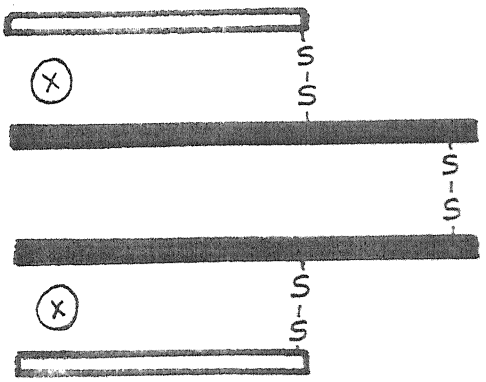

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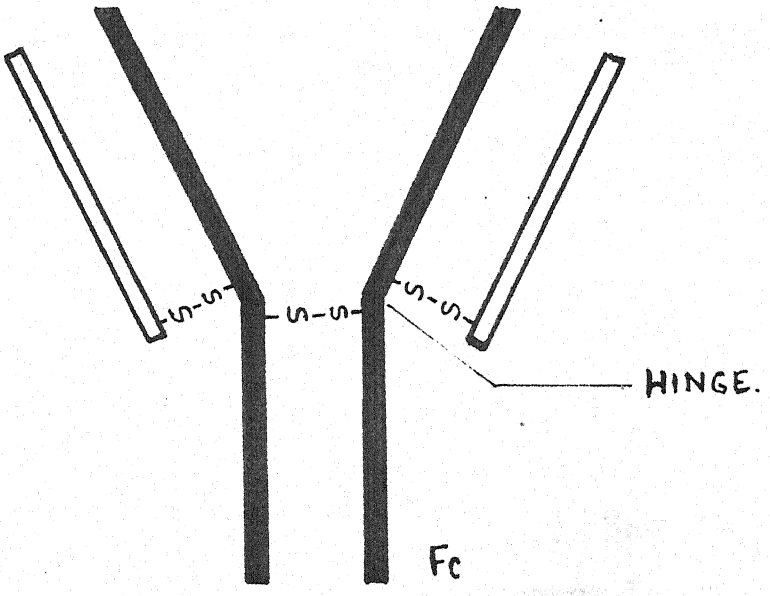
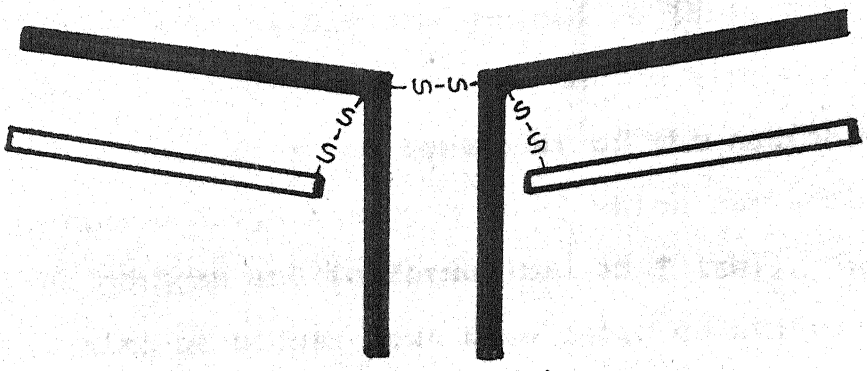




DIAGRAMS SHOWING THE FLEXIBILITY OF IMMUNOGLOBULIN MOLECULE AT THE HINGE REGION.

human ATG is available in purified form and in high concentrations without preservatives, which are likely to damage the CNS.

Immunoglobulins are proteins, the major component of which is IgG with a molecular weight of 150,000. The association of antibody activity with classical gamma globulin fraction of serum was shown many years ago by Tiselius and Kabat. In each species the immunoglobulin molecules can be subdivided into different classes on the basis of their back bone structure. In human, five major types can be distinguished - IgG, IgM, IgA, IgD and IgE. The immunoglobulins can be split by papin into three fragments. Two of these are identical and are able to combine with antigen to form a soluble complex which will not precipitate. These are therefore, univalent antibody fragments and are given the nomeclature Fab(Fragment antigen binding). The third fragment has no power to combine with antigen and termed Fc (Fragment crystallizable). Another proteolytic enzyme pepsin separates the Fc part from the remainder of the antibody molecule leaving a large fragment (5 S) which can still precipitate with antigen and is formulated as $F(ab)_2$. Antibodies can also be broken down into their constituent peptide chains. Firstthe disulphide bonds linking the different chains must be broken by reduction with excess of a

sulphydryl reagent. The reduced molecule has a sedimentation coefficient of 7 S because the chains are held together by non-covalent bonds but they can be separated by lowering the pH, into two peptide chains termed light and heavy chains. Purified IgG antibodies when visualized in the electron microscope by negative staining can be seen to be gamma shaped molecule whose arms can swing out to an angle of 130^{o} through the papin and pepsin sensitive regions acting as hinge. Amino acid analysis of the hinge region has revealed large number of protein residues because of its structure proline prevents the peptide chain assuming alpha helix conformation and so this strength of the chain is extended and accessible to proteolytic enzymes.

LIGHT CHAINS

A convenient source of human material is the urinary Bence - Jones protein which is found in a preparation of patient with myeloma in the synthesis of the myeloma protein. Light chain could be divided into two groups called keppa (K) and Lambda (λ) depending on their reaction with antisera. Approximately 65% of the immunoglobulin molecule in normal serum are of K type and remainder being Lambda type.

HEAVY CHAINS

Studies using antisera prepared against normal and myeloma proteins have established the existence of five major types of heavy chains in the IgD and IgE. But whereas each immunoglobulin class is associated with a particular type of heavy chain they all have K and lambda light chains.

Ig G

During the secondary response, IgG is the major immunoglobulin to be synthesized. Through its ability to cross the placenta provides a major line of defence, against infection for the first few weeks of life. IgG diffuses more readily into the extravascular body spaces. IgG antibodies act by stimulating the ingestion of micro organism through phagocytes.

Ig A

Ig A appears selectively in the seromucosal secretion such as saliva, tears, nasal fluid, sweat, colostrum and secretions of lung, genito-urinary and gastro-intestinal tract. It is present in these fluids as a dimer, where it has the job of defending the exposed external surfaces. IgA function by inhibiting the adherence of coated micro organisms to the surface of mucosal cells, thereby preventing the entry into body tissues.

Ig M

It is referred as macroglobulin antibodies because of their high molecular weight. IgM molecules are polymers of five four peptide subunits each bearing on the extra CH domain. The theoretical combining valency is 10 but this is only observed on inter action with small haptens, with larger antigens. The effective valency fall to 5.

Ig E

Only very low concentration of IgE are present in serum and only a small proportion of the plasma cells in the body are synthesizing this immunoglobulins. IgE antibodies remains firmly fixed for extended when injected into human skin where they are probably bound to mast cells. Contact with antigen leads to degranulation of mast cells with release of vasoactive amines. The main physiological role of IgE appears to be protection of the external mucosal surface of body by local requirement of plasma factors and effector cells through triggering an acute inflammatory reaction

Post mortem findings have revealed changes in liver and haemorrhages in brain, adrenals and spleen. The cause of these haemorrhages is not very evident. The haemorrhages may be due to septicemia as in most

of the cases secondary organisms have been cultured from blood. The role of tetanolysin has not been indicated so far. Tetanolysin may be in some way contributing to the haemorrhagic tendencies in these cases. More stress is laid on tetano spasmin as it causes the evident clinical signs of rigidity and spasm in the body leading to exhaustion which may be the cause of death.

This study has been conducted to prove the efficacy of human antitetanus globulins in the management of tetanus when administered intrathecally.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The disease tetanus prevails in every part of the world and is known by different names in different countries. It is known as "Dhanurvata(India), 'Hausa'(Nigeria), 'Mal de arco' (Maxico), 'Disease of seventh day' (Algenia) and 'Po-shian fong'(China).

In ancient India Charak described tetanus as 'wind disease'. Hippocrates in 460 BC described the poor prognosis of disease. In 1884 Nicolaier isolated the clostridium tetani. Evidence regarding the central action of bacillus was produced by Morax (1902). Wright (1956) confirmed the passage of toxin though the nerve roots.

In the year 1890, Von-Behring and Kittasato produced the successful immunization against tetanus by repeated injections of small doses of toxin and neutralization of toxins by specific antisera. Roman and Zoeller (1933) introduced the antitoxin for human use. Baver suggested that the pregnant women can be immunized to protect the new born infants.

As one moves from polar areas toward the equator, the morbidity and mortality gradually increases with its peak in the tropical and subtropical countries. In India, the annual incidence rate of tetanus during the year 1973-1982 was about 6.7 per lacs population (Sokhney, 1983).

TETANUS NEONATORUM

Although tetanus can occur at any age but new borns are at greater risk because of unhygeinic practices of delivery, lack of immunization of mothers, faulty practices of cord cutting and application of different substances over cut end of cord e.g. mustard oil, ash, cow dung etc. Tetanus neonatorum ranks fifth (Rigby, 1960) among the causes of neonatal deaths in different parts of the world. In rural India tetanus neonatorum is rated as the second commonest cause of neonatal mortality (Shah and Udani, 1962).

According to sample surveys neonatal tetanus mortality rates in 1981 were estimated as 13.3 per 1000 live birth in rural areas and 3.2 in the urban areas in India (Sokhey et al, 1982). In the 1950's and 1960's the recorded neonatal mortality rate varied from 2 per 1000 live births to 120/1000 live births in the world (Miller, 1972).

The special surveys conducted by Basu(1982) and Sokhey (1982) have shown that the tetanus neonatorum prevails in all the 14 states and Union territories of India. Neonatal tetanus mortality has been reported to be higher in the rural areas as compared to their urban counterparts. Tetanus as a cause of neonatal death ranged from 0 to 68.7% in urban areas and from

16.4% to 72.5% in the rural areas. According to Sharma et al (1984) case fatality rate of tetanus neonatorum in rural areas was around 97% and 80% in the urban areas.

The neonatal tetanus mortality rate per 1000 live births was found to be 66.7% in rural Uttar Pradesh, 15.3% in Urban U.P., 4.7% in rural Maharashtra 4.9% in urban Maharashtra, 8.4% in rural Haryana and 1% in Delhi according to a recent national wide survey (Basu and Sokhey, 1982).

Neonatal mortality was found to be 20 per 1000 live births in Madhya Pradesh. In the rural areas of Rajasthan and west Bengal the neonatal mortality from tetanus rated between 20 and 10 per 1000 live births (Sokhey et al, 1983). It was recorded as a cause in 1/3rd or more neonatal deaths in Bihar(rural/urban), Kerala (rural/urban) and Tamil Nadu (rural).

TETANUS IN CHILDREN

Athavale et al (1974) observed that the maximum number of cases in children were between 2 to 5 years of age and they constituted 39% of total cases in children. 74% of the cases in children resulted from Otorrhoea and injury.

Jolly et al (1974) noted a mortality of 37.69% due to tetanus in children. According to Athavale (1974) in 20.7% children the causative factor

could not be determined. Athavale et al (1974) reported a high mortality of about 50% in cases of tetanus following burns and vaccination and mortality was minimum in cases with otorrhoea as the causative factor.

TETANUS IN ADULTS

This includes patients beyond 12 years of age. Jolly et al(1974) observed that the maximum incidence of adult tetanus was in the age group of 21 to 30 years (23%). The highest mortality due to tetanus in adults was observed in the age group of 41 to 50 years(76.47%). A very high incidence of tetanus has been noted in Punjab. It was 90.4%100,000 cases per year (Gorden et al, 1961). Injury has been noted as an etiological factor in most of the cases of adult tetanus (38%) but the cause could not be detected in significantly large number of cases (35.5%) (Jolly et al, 1974).

SEX RELATION OF TETANUS

The prevalence and mortality rate of tetanus is higher in males than in females in all the ages (Modi, 1965). Males appears to be the more sensitive to tetanus toxin than females (Kacharevie, 1952). But Indira Bai et al (1975) found lower mortality rate in males (74.0%) than females (88.0%).

RURAL AND URBAN TETANUS

Tetanus mortality has been reported to be higher in patients belonging to rural areas as compared to their urban counterpart. According to Sokhey et al (1983) the mortality due to tetanus ranged from 0 to 68.7% in urban areas and 16.4% to 72.5% in the rural areas. Stanfield et al (1973) also noted a significant rural/urban difference in tetanus mortality. It was 67 per thousand live birth in rural Uttar Pradesh as compared to 15 per 1000 live births in urban Uttar Pradesh. In an urban centre like Delhi the mortality was 1 (Basu et al, 1982).

SEASONAL VARIATION OF TETANUS

Bhat et al (1979) have reported that maximum number of cases of tetanus neonatorum were admitted during the monsoon season i.e. between June and October. They attributed this increased incidence to the greater risk of contamination and infection during this season. Gupta et al(1977) have reported a higher incidence of tetanus during rainy season. However, Vakil et al (1964) found no significant seasonal variation.

PUERPERAL TETANUS

A high incidence of postpartum and post abortal tetanus is due to faulty and unhygienic

practices of deliveries, poor post partum care and unhygienically conducted illegal abortions.

The mortality rates due to puerperal tetanus varies from 49% to 100%. According to the observations of Srivastava and Chatterji (1961), Shah et al (1962) and Bhatt (1962) puerperal tetanus contributes 10 to 12.7% of all cases.

SOCIAL FACTORS

Sanders et al (1974) have found that tetanus had a high prevalence among the under nourished, rural based and poor individuals who were working as cultivators or agricultural labourers. Illiteracy was rampant in such a population and they lived in a crowded atmosphere, in close contact with cattles and pigs.

In new guinea, women during childbirth and puerperium are considered unclean and are forced to live in "Menstrual houses" where no one can visit them. In India also the woman is considered untouchable during the first 10 days of childbirth. Jolly et al (1974) have noted an excessive prevalence of tetanus in Punjab. He attributed this to Punjab being predominantly an agricultural state and that there exists a very close contact between the animals and human population in the rural areas.

The incidence of tetanus neonatorum varies inversely with the development of MCH services and

obstetrical services. In the developing countries midwifery is still practised by untrained midwives or local elderly women. They are known as dais in India. 'dukun in Indonesia and 'Montamyal' in Thailand (Bytchenko, 1966).

Nowell et al (1966) observed the highest rate of 95 tetanus cases per 100 births in neonates delivered by a blind midwive in Gauchene, Columbia, South America.

INCUBATION PERIOD

It is defined as the timeinterval between the entry of the organism in the host and the appearance of the first symptom. In tetanus neonatorum this period corresponds to the age of baby in most cases (Athavale, et al, 1974).

Joffari et al (1966) and Beaty (1980) noted high mortality with short incubation period specially if it is less than 7 days.

PERIOD OF ONSET

It is the interval between the first symptom and the onset of first spasm. It is supposed to be the most reliable index (Cole, 1940) from prognosis point of view. Cole (1940) found that a short period of onset was associated with worse prognosis. Similar observations have been noted by Athavale et al (1974).

Jolly et al; 1974; Bhatt et al, 1962; Phatak et al, 1973; and Patel et al, 1960).

ORGANISM AND PATHOGENESIS

The clostridium tetani is a gram positive spore bearing obligatory anerobic bacillus. Spores are present usually at the terminal end of the bacillus which gives a drum strick appearance to the organism. It produces two distinct toxins - (1) tetanospasmin (Neurotoxin) and (2) tetanolysin. Tetanospasmin is a selective neurotoxin with a molecular weight of about 67000.

PATHWAY OF TETANUS TOXIN IN C.N.S.

The toxin tetanospasmin is produced locally and is absorbed by the motor nerve endings. Then it is transported to central nervous system along the peripheral nerves. The neural pathway of the spread of toxin to the central nervous system has the following links :

Neural motor endings in muscle - Muscle nerve- anterior roots - anterior horn cells of the spinal cord or motor neuclei in the brain stem (Kryzhanovsky).

The toxin enters the C.N.S. by two pathways :

1. Regional neural pathway.
2. General neural pathway.

The clinical features of the disease depends upon which pathway has been involved in the toxin

transport to C.N.S., if the toxin enters by the regional pathway, there arises a local and ascending tetanus in animals and partial tetanus in human. Such condition may arise if the toxin spread is locked by antitoxin.

The general neural pathway represents the sum of regional neural pathways, from all the muscles. When toxin enters the blood it enters all the muscles and then through the general neural pathway enters the C.N.S.. In such a condition the toxin first enters the motor nuclei and travels through the shorted neural pathways to the muscles of head and face giving the typical features like Risus Sardonicus and trismus. The toxin enters the C.N.S. by longer neural pathways to produce opisthotonous and generalized rigidity. This is known as tetanus descending (Kryzhanovsky, 1974).

BINDING OF TOXIN BY BRAIN TISSUE

The receptors for the tetanus toxin in the brain substance is represented by gangliosides forming a complex with the cerebrosides (Heyningen, 1959) aided by the sialic acid in gangliosides (Mellanby et al,1967). The toxin bound with protagon (the non-purified mixture of gangliosides with cerebrosides obtained from brain substance) retains the capacity of being neutralized by antitoxin without being split from protagon. (Kryzhanovsky et al, 1970).

Tetanus toxin possesses three active functional groups :

1. Antigenic : It ensures binding of toxin with antitoxin.
2. Neurotrophic (Gangliosidotrophic) : Ensures binding with brain receptors.
3. Toxophoric : Ensures the pathogenic effect(Bondertchuk et al, 1971 and Clowes, 1972).

BINDING OF TOXIN BY NEURONAL MEMBRANE

Synaptosomes have the greatest affinity for toxin binding(Mellanby et al, 1965). This is due to the fact that the membrane of synaptosome contain gangliosides (Dehirmenjian et al, 1969). Toxin neutralized by antitoxin is also bound by synaptosomes(Kryzhanovsky et al, 1973).

EFFECT OF TETANUS TOXINS OF THE PRESYNAPTIC APPARATUS

Tetanus toxin acts on the presynaptic apparatus of central synapses in the spinal cord (Curtis et al, 1968) as well as on the neuromuscular junction(Kryzhanovsky et al, 1971, 72). It results in the disturbance of the release of central inhibitory transmitter glycin and GABA as well as excitatory transmitter acetylcholine in the neuromuscular junction. As a result of disturbance of transmitter release there occurs accumulation of a significant number of vesicles containing the transmitter in the axon terminal, in the poisoned neuromuscular synapses(Kryzhanovsky, 1973 and Pozdnyakov OM et al, 1971).

FUNCTIONAL EFFECTS OF TETANUS TOXIN ON SYNAPTIC APPARATUS

As a result of disturbance of transmitter release by the presynaptic apparatus a block of synaptic transmission takes place. The characteristic effect of tetanus toxin on C.N.S. is the disturbance of functioning of the inhibitory synapses and the resulting block of various forms of post synaptic and some form of presynaptic inhibition(Kryzhanovsky et al, 1968; Brooks et al 1957; Curtis, 1959 and Sverdlov, 1960; 69).

PATHOGENESIS OF MUSCLE RIGIDITY AND GENERALISED CONVULSIONS

Muscular rigidity is due to the disturbance of inhibitory process occurring in the system of motoneurons and associated interneurons. As a result the capacity of the efferent output is increased, thepolysynaptic reflexes are enhanced and the periphery receives a strengthened and permanent flow of afferent impulses which produces growing muscular tension, contraction and hypertone (Acheson et al, Davies et al, 1954; Kryzhanovsky, 1965;66).

Convulsions are the result of disturbances of inhibitory mechanisms in the system of spinal interneurons.

FUNCTIONAL CHANGES IN THE VEGETATIVE NERVOUS SYSTEM

Vegetative systems in tetanus such a tachycardia, changes in arterial pressure, increased

BMR, perspiration and hyperthermia indicates the involvement of vegetative nervous system in the pathologic process. Pathogenesis of these changes is not yet clear.

CHANGES IN THE ENDOCRINE SYSTEM

In the course of development of tetanus intoxication the systems involved are hypothalamus and hypophysis and various clinical data have shown a disturbance of the electrolyte and water balance in tetanus (Nikhailov, 1968). In tetanus the metabolism of catecholamines and corticosteroids is also disturbed.

CHANGES IN IMPORTANT VISCERAL SYSTEM

Pulmonary complications are the important cause of death in tetanus. Ultrastructural and microcirculatory changes in lung occur in tetanus intoxication (G.N. Kryzhanovsky, 1973). These changes lead to congestion and pneumonia.

Important myocardial changes occurring in tetanus includes protein and vacuole dystrophy, inhibition of the activity of oxidase, disturbances of microcirculation, intravascular thrombs, perivascular haemorrhage and disturbances of lymphocirculation.

CLINICAL FORMS OF TETANUS

1. **Localized tetanus**

It is due to the localized involvement of a group of muscles of a limb resulting in pain and spasm

of muscles in proximity to the site of injury. This form may convert into generalized tetanus.

2. Generalized tetanus

This results because the generalized rigidity and reflex convulsions. Trismus is the first indication of tonic rigidity and usually the first symptom. Spasm of the masseter muscle leads to locked. Spasm of facial muscles leads to Risus sardonicus. Tonic contraction of spinal and abdominal muscles causes opisthotonous. Generalized convulsions appear as the severity of disease increases.

3. Cephalic tetanus

This usually follows the injuries of face or head specially around orbit but it can occur in cases with injuries to other parts of body and some times without any apparent wound. It carries a good prognosis and mortality is low (Vakil et al, 1964).

This variety of tetanus is associated with paresis or paralysis of one or more of the cranial nerves. It has been seen that the involvement of facial nerve is more common (Vakil et al,1973). Cephalic tetanus remains usually confined to head and neck but may involve the entire body.

DIFFERENTIAL DIAGNOSIS OF TETANUS

Although the disease tetanus can be diagnosed easily due to its certain characteristic features but there are certain conditions which need to be distinguished from tetanus.

1. Meningitis

There is high fever with the signs of meningeal irritation, C.S.F. examination is diagnostic. Trismus is not present.

2. Epilepsy

Patient may loose the consciousness which is momentary there may be involuntary passage of faecus and urine. There may be history of previous seizures. Characteristic features of tetanus are absent.

3. Strychnine poisoning

Patient may gives history of ingestion of broken seeds of NUX vomica. Onset is sudden and in between spasm the muscles are completely relaxed. Chemical analysis of gastric aspirate proves the diagnosis.

4. Neonatal hypoglycemic convulsions

Here the signs of CNS irritation are present like - Jitterness, coarse tremors, twitching and convulsions, apathy and coma may supervene. Intra venous glucose improves the symptoms immediately. Blood glucose estimation is helpful.

PREVENTION OF TETANUS

Tetanus is a preventable disease. It has in fact been suggested by some authors that it can be virtually eliminated by universal immunization. This unfortunately is lacking in our country in the real sense. Consequently there is a high incidence of tetanus in India and particularly in Uttar Pradesh and the adjoining areas of Madhya Pradesh.

Two forms of immunization are available against tetanus.

1. Active immunization.
2. Passive immunization.

1. ACTIVE IMMUNIZATION

This results in a much longer period of immunity as compared to passive immunization. But on the other hand active immunity takes a longer time to develop. Immunity is conferred late to the patient, unfortunately lacking when the patient needs it most, whereas passive immunity provides immediate protective antibodies against tetanus to the patient.

Two vaccines are available for active immunization (1) Plain tetanus toxoid. (ii) Adsorbed vaccine.

Though plain tetanus toxoid is a quite effective vaccine, the incorporation of an immunological adjuvent in the vaccine such as aluminium hydroxide confers a number of advantages on this adsorbed vaccine -

a. The immunity develops more quickly after using adsorbed toxoid. Immunity develops within 4 to 5

weeks of administration of adsorbed vaccine (Smith J.W.G.), while the plain variety may take a longer time.

b. The immunity stimulated by the adsorbed toxoid reaches a higher level and is longer lasting than the plain toxoid.

c. When administered concurrently with passive immunization, the adsorbed toxoid is more reliable. With plain toxoid, the injected antitoxin may interfere with the development of active immunity, but interference with aluminium hydroxide adsorbed toxoid is minimal (Smith, J.W.G., 1974).

Plain tetanus toxoid consequently finds little place nowadasy in tetanus prophylaxis as the adsorbed vaccine stimulates a quicker, higher and more durable immunity than plain toxoid.

REACTIONS TO TETANUS TOXOID

These may be generalised or localised but are relatively uncommon. Local reactions were found to have a higher incidence in women as compared to men

Generalized reactions may manifest as fever malaise etc. but are uncommon. Reactions resembling anaphylaxis or serum sickness are very rare.

Local reactions to tetanus toxoid are not serious and usually consist of local pain and tenderness accompanied with an area of visible erythema and

swelling between 2 and 5 cms in diameter usually. Sometimes such reactions may become more marked with tenderness or swelling of the whole of the upper arm (where it is usually injected). However, these reactions usually subside within 2-3 days.

IMMUNIZATION SCHEDULE AGAINST TETANUS

This process should be stated right from the stage of pregnancy when the fetus and mother are both provided with immunity by vaccination of the mother. Transplacental passage of maternal antitoxin prevents tetanus neonatorum. The active immunity produced in the mother prevents post partum/abortion tetanus. The accepted protective level of antitoxin titre is 0.01 I.U. of tetanus antitoxin per millilitre of cord blood (Maclennan et al, 1965).

In pregnancy, the recent schedule for immunization is the administration of two doses of adsorbed tetanus toxoid, the first at 7 months of pregnancy and the second at 8 months.

In the newborn child the first dose of vaccine in the form of D.P.T. (Triple vaccine) should be administered within 2 to 3 months of birth. It should be followed by two more doses at 4 to 6 weeks interval. A 4th dose should be given after one year of third dose. A booster is required at intervals of 10 years. School

going children should be immunized with 3 doses of tetanus and diphtheria toxoids starting from the age of 5 years, if already immunized earlier during infancy (even earlier if unimmunized before). The second dose should be given at 4-6 weeks after the first dose and the third dose 6 months to 1 year after the second dose. A booster is required every 6 to 10 years (Smith et al). In adults also a similar regime is followed starting at any age, as required.

A newer type of vaccine containing 3 times more potency (17.5 Lf as compared to normal 5 Lf by the ordinary toxoid) has been found to be very effective by only a single dose of toxoid. It takes 12 months for appropriate protective response to develop(Breman et al, 1981).

Recently Talwar (1985) has developed a double acting vaccine against pregnancy and tetanus. Such a vaccine produces antibodies acting against human chorionic gonodotropic hormone and also against tetanus toxin.

PASSIVE IMMUNIZATION

This is available in two forms :

1. The equine antitoxin (A.T.S.) antitetanus serum.
2. Human antitetanus immunoglobulin.

This type of immunization confers immediate protection against tetanus and is particularly useful

in tetanus prone situation, especially after exposure. The human form (T.I.G.) is devoid of any reaction or complications whereas the equine form (A.T.S.), does produce at times severe sensitivity reactions and anaphylaxis. It is therefore administered after appropriate sensitivity tests. Unfortunately the protection provided by passive vaccination is very short lasting.

Human anti tetanus immunoglobulin (T.I.G.) is administered in a dose of 250 I.U. deep I.M.. It ensures serum antibody levels of 0.01 unit/ml in all patients for 28 days or more. This may be combined with adsorbed tetanus toxoid (in a dose of 10 Lf) for active-passive immunization.

A.T.S. (antitetanus serum) is administered in doses of 1500 I.U. to 6000 I.U. i.m. after sensitivity tests.

MANAGEMENT OF TETANUS CASES

- A differential count examination of W.B.C. reveals granulocytosis in one third of the patients.
- Microscopic examination of pus or necrotic material may reveal bacilli (tetanus) with spores in 30% of cases. Culture methods are more reliable.
- Sometimes raised levels of serum aldolase and Serum Creatinine Phosphokinase are found. These may be diagnostic (Mullan et al, 1964).

- All electrocardiographic record usually shows sinus tachycardia.

THERAPY

The treatment policy in tetanus is as follows :

I(a) Neutralisation of unfixed toxins - tetanus antitoxin (T.I.G./A.T.S.).

(b) Elimination of the toxin source - local measures.

(c) Control of convulsions and muscle rigidity.

(d) Maintenance of adequate airway and ventilation.

(e) Symptomatic treatment and nursing care.

(f) Treatment of complications.

II. Prevention of recurrence.

III. Prophylaxis.

NEUTRALISATION OF THE TOXIN

Anti-tetanus Serum (A.T.S.)

Over the years tetanus antitoxin in the form of equine antitetanic serum (A.T.S.) has been used by various routes for the treatment of tetanus. Sherrington (1917) demonstrated the efficacy of intrathecal A.T.S. in monkeys. Ildirim (1974) and Sanders et al (1977) noted the efficacy of intrathecal A.T.S. along with parentral steroids in humans. However some have doubted its usefulness. Neefuaye et al found that A.T.S. failed to improve survival in neonates despite its intrathecal use.

Bryant and Fairman (1940) were of the opinion that A.T.S. has a controversial role in tetanus therapy besides producing allergic reactions. Damage to the C.N.S. by the preservatives used in it have discouraged its use. Pratt even suggested that intrathecal administration of A.T.S. should be stopped.

It has been suggested that antitetanus serum (A.T.S.) doesnot neutralize tetanus toxin already fixed in the C.N.S. and does little to ameliorate symptoms already present.

HUMAN ANTITETANUS IMMUNOGLOBULIN

This specific antitetanus hyperimmune globulin (human) is obtained by fractionation of Hepatitis-B surface antigen and AIDS antibody negative plasma, of human donors hyperimmunized with tetanus toxoid. This immunoglobulin is further purified by affinity chromatography, column chromatography and gel filtration techniques. Optimal purity of above 99% can be obtained. This is tested by immunoelectrophoresis.

Presentation

Anti tetanus human immunoglobulin (T.I.G.) is available in two strengths. 1. Ampoules containing TIG in a liquid form of 250 I.U. strength. 2. Vials containing 500 I.U. of TIG in a freeze dried powder form, along with diluent.

Advantages of Antitetanus Human Immunoglobulin

1. There is no risk of sensitization to heterologous protein - since TIG is of human origin it is virtually free from the risk of inducing hypersensitivity reactions unlike ATS which is of equine origin containing heterologous protein and hence having greater risk of hypersensitivity reaction.
2. Antibody levels of the homologous(human) TIG persist considerably longer than the heterologous(equine) ATS. The half life of TIG is 20 to 40 days, while it is only 7 to 14 days in case of ATS, hence TIG protects longer.
3. Antitetanus human immunoglobulin doesnot interfere with patients antibody production.
4. It does not require sensitivity tests.
5. TIG is devoid of any preservative and lyophilized. It can be thus used intrathecally.

For therapeutic purposes 3000 I.U. to 6000 I.U. of TIG have been recommended deep intramuscularly. For more rapid action part of this can be given intrathecally In children some authors have recommended a dose of 4 units/kg body weight. However it is logical to administer at least 250 I.U. regardless of age of the child, since theoretically the same amount of toxin will be produced in the child by the clostridia as in adults. Gupta et al (1980) recommended a dose of 250 I.U. intrathecally.

Varying results have been reported on the use of intrathecal TIG Gupta et al (1980) found that intrathecal TIG was useful in reducing mortality in patients with mild tetanus. He found that in patients who were given TIG by IM route had a higher mortality. Chopta et al (1986) pointed the usefulness of intrathecal TIG in high doses in more severe cases of tetanus.

Contrary to the above Wakil et al (1977) found no difference in mortality in adult tetanus patients who received intrathecal TIG . Chugh et al (1985) also found no beneficial response of intrathecal TIG in neonatal tetanus.

It has been postulated that the initial spasms are due to the tetanus toxins circulating free in the CSF not yet fixed to anterior horn cells. Thus free toxin is available for neutralisation by intrathecal tetanus antitoxin which circumvents the blood brain barrier. But probably after 48 hours when the toxin is presumed to be fixed to the nervous tissue, intrathecal antitoxin is not of much value (Sanders et al, 1977).

Other use of TIG

- It is useful in all tetanus prone wounds as in crush injuries, compound fractures and accidental cases particularly if there is no clear evidence of prior immunization

- In pre-operative preparations especially in emergency surgery.
- In uncovered cases of M.T.P. and septic abortions.
- In previously immunized mothers, when given during the antepartum period prior to delivery it provides dual protection to the mother and fetus. TIG being 7S type crosses the placental barrier giving protection to the fetus besides the mother.

ELIMINATION OF THE TOXIN SOURCE - LOCAL MEASURES

This is a very important step in the management of tetanus. It has been suggested by some authors that if wound toilet is properly performed within 6 hours of injury it will destroy the spores. But wound toilet alone if performed after 6 hours fails to prevent tetanus. However, meticulous toileting is still essential to prevent further absorption of toxins. Proper wound debridement should be carried out as soon as possible. Grossly contaminated wounds need to be cleaned with hydrogen peroxide solution. Use of local antibiotics may also be effective. In case of suppuration all pus should be drained out and wound cleaned.

In neonates the umbilical cord should be handled with all aspetic and antiseptic precautions. The cord should be cleaned with spirit and 1% gention violet paint should be applied. Bar einfections need to be taken care of promptly. Any discharge should be

cleaned with spirit swabs and ear kept dry. Handling with dirty hands or entry of water and the instillation of any household medicament in the ear needs to be stopped. Appropriate antibiotic and if necessary local ear drops should be used.

CHEMOTHERAPY

Antibiotics notably Penicillin are quite effective against Clostridium tetani and their use similarly has been thought to affect the outcome favourably (Parcy et al, 1985). The usefulness of Penicillin has also been suggested by Bhat et al (1979) and Bhandari (1980).

In a patient sensitive to Penicillin, Kanamycin in two divided doses of 10 mg/kg body weight may be used.

Metronidazole is effective against anaerobic bacteria. Some have pointed its usefullness in the disease.

CONTROL OF CONVULSIONS AND MUSCLE RIGIDITY

The control of muscle spasms is one of the most important factors in the prognosis of patients with severe tetanus.

Many muscle relaxants have been advocated but some have their own demerits. To name a few-centrally acting muscle relaxants like methocarbamol, mephenesin,

meprobromate etc; peripheral muscle relaxants like d-tubocurarine, succinylcholine, mytolon etc. Peripheral muscle relaxants are usually administered alongwith I.P.P.V.

Mephenesin is an effective muscle relaxant when given intravenously. Its drawback is that it causes hypotension and sometimes haemoglobinuria.

Meprobromate has been described as one of the most effective drugs in relieving muscle spasticity (Nyguist et al). It has a prolonged action. However, it has the disadvantage of causing thrombosis, hemolysis and possibly, glomerular damage on intravenous therapy.

Methocarbamol appears to possess the ideal pharmacological action to control the muscle spasm induced by tetanus toxin. It has a greater potency and acts for a longer duration (Grandal et al, 1960).

It has the added advantage of suppressiong spasms without appreciable suppression of respiration. The dose is 2 to 20 gm per day by intravenous infusion or orally in divided doses.

Diazepam : In addition to being a hypnotic, diazepam is a potent muscle relaxant. It acts by depressing the ascending reticular activating system and internuncial neurons. Hendrickse and Sherman found that diazepam was very effective in controlling convulsive aspasms during the early phase of treatment. Kazim

reported that intravenous diazepam relieved opisthotonos but the effect lasted slightly more than an hour. Benjamin and Baltimore (1968) recommended diazepam as an alternative to phenobarbital or phenothiazines. He found that parentral diazepam was very useful.

However, a combination of nuscle relaxants has been found to be more effective than massive dose of any single drug (Jolly et al, 1973). Diazepam was first used in combination with chlorpromazine by Hendrickse et al (1965).

Maintenance of Airway and Tracheostomy

Maintenance of a clean airway and adequate ventilation is of utmost importance in tetanus care. All secretions should be aspirated by suction. The mouth and nasal cavities should be kept as clean as possible. All froth should be cleaned. Children and neonates should be nursed with their head on one side to prevent aspiration of fluids into lungs. If necessary endotracheal intubation may be carried out. If it is not possible then tracheostomy should be performed. The indication for tracheostomy is either laryngospasm or copious secretions. Endotracheal suction can then be carried out. However, care of tracheostomy is then required.

The need ffor tracheostomy should be recognised early and should rather be performed electively than as

an emergency procedure. Shah et al (1984) found a mortality of 19.26% with tracheostomy. However the drawback is that it needs meticulous post-tracheostomy care and trained nursing personnel for its management.

Oxygen inhalation should be given as and when necessary.

TOTAL PARALYSIS AND VENTILATION

In severe tetanus complete muscular relaxation (paralysis with peripheral muscle relaxants e.g. d-tubocurarine) combined with tracheostomy and intermittent positive pressure ventilation (I.P.P.V.) has been a landmark in tetanus therapy.

Lassen (1953), Smith et al (1956) and Hendrickse et al (1966) have reported favourably on the use of tracheostomy, total paralysis and I.P.P.V.

However, only limited effectiveness has been claimed by Alhaudy et al, by this regime. Sinha and Athavale found this type of treatment unsuitable in India on account of its cumbersomeness, costs and the need of skilled medical and paramedical personnel.

GENERAL MANAGEMENT AND NURSING CARE

The patients should be nursed in an isolated quiet and calm environment to cut off all external stimuli. Adequate care of bowel, back and bladder is required. Frequent turning in bed alongwith the

application of powder and spirit to clean the back is necessary to prevent bedsores. The patient should be catheterized to avoid possible urinary retension and incontinence. Appropriate antibiotic coverage may be given and should be changed according to culture and sensitivity reports. Constipation should be taken care of with suppositories or low enemata as necessary.

Oral nutrition is maintained as far as possible. However, if dysphagia increases intravenous fluids are given and oral supplementation stopped till protective reflexes of swallowing and coughing are present. If necessary Ryles tube feeding may be supplemented.

As regards fluid requirements a minimum fluid intake of 130 ml/kg in children under 6 years per day and 80-130 ml/kg/day in older children has been recommended (Kerr J.H.) In adults the amount should be regulated in relation to urine output and fluid losses. This may vary from 1.5 to 4 litres per day as necessary under the circumstances.

Small daily fluid deficits may accumulate to produce subclinical dehydration (Kerr J.H., 1979). As such it may be produced by fluid losses in saliva and sweating. Hence it is important to maintain adequate hydration.

OTHER MISCELLANEOUS FORMS OF THERAPY

Corticosteroids

Sanders et al have pointed the usefulness of steroids in tetanus therapy, in particulars betamethasone. The explanations given by them were that -

1. Part of the action of betamethasone is antihistaminic. This results in reduction of pericellular oedema around motor nerves and ganglions.
2. It is possible that betamethasone either reduces the amount of acetylcholine produced, or inhibits its action (Fal W. et al, 1963). Betamethasone may also support a failing supra renal function (Sanders et al, 1966).
3. Betamethasone may have an antitoxaemic action in tetanus.

Beta-blockers

Sainani et al (1972) found that the tetanus toxin has beta stimulant effect on the frog's heart and and this effect could be blocked by propranolol (beta-blockers). Kerr et al (1979) observed that there was sympathetic overactivity in tetanus patients. This sympathetic overactivity manifested as disproportionate tachycardia, fluctuating high blood pressure and profuse sweating. Such patients having features of sympathetic overactivity when treated with beta-adrenergic blocking drugs showed improvement (Kerr et al, 1979).

However, the role of beta blockers is disputed and still under clinical trial. The literature now contains that removing sympathetic stimuli to the heart may remove the ability to sustain adequate blood flow through the constricted peripheral vasculature (Edmonton et al, 1979).

CHOLINESTERASE RESTORING THERAPY

Leonardi et al observed that the tetanus toxin had an anticholinesterase effect somewhat similar to organophosphorus agents and that antidotes to such agents. the oxime group of compounds could, by their cholinesterase restoring action, be of benefit in tetanus therapy. They used pralidoxime methanosulphonate 40 mg/kg/day together with vitamin B_{12} in a dose of 100 mg/kg/day for 10 days intramuscularly and found it to be of some benefit. But this still requires further trails.

HYPERBARIC OXYGENATION

In a trial conducted by Pascale et al, it was observed that there was active regression of symptoms following hyperbaric oxygen therapy. The progression of the disease was arrested and reversed. However its use is limited, owing to its limited availability in hospitals. Furthermore, it requires more trials.

PROGNOSTIC FACTORS

Age : Vaishnava et al found that the survival rate was influenced by the patients age. In children

and adult patients he found that higher the age, the worse was the prognosis. In neonates the lesser the age at the time of admission the worse is the prognosis (Phatak et al, Bhat et al).

Sex : Vaishnava et al, found no difference in the mortality in two sexes. Vakil et al (1976) also found a similar observation. However, Modi (1965) found a higher mortality in males.

Incubation period : Mortality varies inversely with the incubation period. The longer the incubation period, the lesser is the mortality (Patel et al, 1965; Vakil, 1964).

Period of onset: Mortality increases with shorter period of onset (Patel et al, 1959; Vaishnava et al, 1966 and Cole , 1940).

Severity of convulsions : Mortality increases with increasing severity of convulsions (Bhandari et al, 1980; Bhat et al, 1979; Shrivastava et al,; Shah et al).

Fever : Fever has been reported as a bad prognostic sign (Bhandari et al, Spaeth et al).

COMPLICATIONS AND CAUSES OF DEATH

Oversedation is one of the major complications of the treatment given (Sehgal et al, 1978). Respiratory complications including aspiration pneumonia are very important and commonly encountered complications

(Sehgal et al, 1978; Bhatt et al, 1968; Athavale et al). Injection abscess may occur occasionally (Sehgal et al, 1978). Parotitis has also been reported by some workers (Athavale et al, 1974; Bhatt et al, 1962). Other complications include hyperpyrexia, constipation, thrombophlebitis, electrolyte imbalance, bed sores, septicemia and retention of urine (Bhatt et al, 1962).

Athavale et al (1974) have reported dehydration, acidosis facial palsy and compression fracture of vertebrae as important complications.

Respiratory spasms with apnoeic spells are the commonest cause of death (Athavale et al, Bhat et al, 1962). Death may also occur due to hyperpyrexia, laryngeal spasm, laryngeal or pulmonary oedema, electrolyte imbalance, hypoxia etc. However all of the above complications may contribute to death, although some of the complications may be reversed when diagnosed and treated early and the patient may be saved.

MATERIAL AND METHODS

MATERIAL AND METHODS

The present study was conducted in the M.L.B. Medical College, Hospital, Jhansi (UP). This study includes a combined retrospective and prospective analysis of tetanus cases admitted in tetanus ward during January, 1985 to June, 1989.

The objects of this study were :

1. To establish the role of human antitetanus globulins in the management of tetanus.
2. To study the clinical pattern of disease in Bundelkhand region.
3. To evaluate and compare the mortality pattern of tetanus in Bundelkhand region with that of India and other developing countries.

The cases of tetanus were categorized into three groups :

I. Neonates : Cases from 1 day to 1 month of age.

II. Children group - included the cases from 1 month to 12 years of age.

III. Adult group - included all the cases above the 12 years of age.

Every case was subjected to a thorough history and clinical examination as listed below :

A. HISTORY

In history specific points were recorded like

mode of injury, history of umbilical cord sepsis, ear discharge, child birth, period of onset, incubation period, previous prophylaxis against tetanus and treatment taken before hospitalization.

In cases of tetanus neonatorum, the enquiry was made regarding the instrument by which umbilical cord was divided, the material used for cord ligation and substance applied over the cut end of cord.

B. PHYSICAL EXAMINATION

This consisted of general examination and special examination. General examination included the following points :

- Pulse/min.
- Temperature ^{o}F
- Blood pressure
- Respiratory rate/min.
- Respiratory distress, if any.
- Hydration.
- Cyanosis
- Oedema
- Lymphadenopathy.
- Constipation.
- Retention of urine

Special Examination

- Risus Sardonicus.
- Neck rigidity.
- Opisthotonous
- Lock jaw
- Dysphagia
- Reflex spasm
- Convulsions/Spasm
- Position of limbs
- Eyes
- Abdominal rigidity
- Local examination in cases of septic focus or wound.

In cases of tetanus neonatorum some additional factors were noted like prematurity, inability to swallow the milk, body weight and umbilical cord sepsis.

Criterion of Patel and Joag (1959) was followed for assessing the severity of disease.

Criterion I : Presence of locked jaw(inability to suck).

II : Presence of spasm.

III : Period of onset 48 hours or less.

IV : Incubation period of 7 days or less.

V : Axillary temperature of 99°F or rectal temperature more than 100°F.

On admission or within 24 hours of admission.

One point was given for each criterion. The cases having one of the five criterion were termed as grade I. The cases having only two of the five criterion were graded as grade II and so on.

C. INVESTIGATIONS

Cases were subjected to following investigations :

1. Routine blood examination.
2. Platelet count.
3. C.S.F. examination.
4. Liver function tests.
5. Culture & sensitivity of umbilical cord.

D. TREATMENT

Treatment was divided into two main parts :

II. General Treatment

1. General nursing care including the care of bowel, bladder and back.
2. Maintenance of airway.
3. Intravenous/Ryle's tube/Oral route to fulfil the nutritional requirement depending on patient's condition.
4. Care of local wound if any/care of umbilical cord in neonates.
5. Sedation was maintained by using Diazepam, Promethasine hydrochloride and chlorpromazine in appropriate doses by intravenous, intramuscular or oral route.
6. Muscle relaxant methacarbamol was used to reduce spasm.
7. Antibiotics were given according to need like crystalline penicillin, Ampicilline, Gentamycin, Chloromycetin and Septran.
8. In cases of post partum tetanus and with gross infection the metronidazole I/V or oral was used.

II. Local Treatment

In cases of neonates it included the cleaning and dressing of umbilical cord. In cases of ear discharge it included the thorough cleaning of ear and local instillation of antibiotic drops. In cases of

wounds cleaning, debridement and dressing of wound was done regularly.

III. Specific Therapy

Specific therapy was provided by using human antitetanus globulin (ATG) administered via intrathecal route. For administering the ATG by intrathecal route the lumbar puncture was performed between L4-L5 vertebral under aseptic conditions. Under the coverage of mild sedative (Diazepam) and muscle relaxant(Methacarbamol). After introducing the lumbar puncture needle in the canal 8-10 drops of cerebrospinal fluid was allowed to drain out then human ATG was slowly injected via the L.P. needle in the intrathecal space. The doses of ATG varied from 250 I.U. to 1000 I.U. or more depending upon the availability of ATG.

According to treatment given the total cases were kept in 4 groups :

- In one group cases were kept who received ATS of equine origins. These patients were belonging to retrospective study and they received ATS in varying doses from 10,000 units to 1 lacs I/V and intramuscularly.
- In second group these cases were kept who received intrathecal human tetanus immunoglobulins.

- In third group cases ~~those~~ were kept who received intramuscular human tetanus immunoglobulins.
- In fourth group, those cases were kept who did not receive any specific treatment due to some reasons.

IMMUNIZATION

All the patients were immunized actively with tetanus toxoid. 0.5 ml intramuscularly according to the doses schedule recommended by W.H.O. :

1st dose : At the time of admission.
2nd dose : 6 weeks after the 1st dose.
3rd dose : 6 months after the 2nd dose.

A booster dose was advised 10 years after the primary course of immunization.

OBSERVATIONS

TABLE 1 : Showing yearly admission and deaths of tetanus cases.

Year	Total admission	Total deaths	Total cases of tetanus		Deaths in tetanus cases	
			No.	%	No.	%
1985	21000	1241	224	1.06	111	8.94
1986	20664	1191	205	0.99	78	6.54
1987	19371	1122	138	0.71	60	5.34
1988	23530	1452	285	1.21	126	8.67
Upto June 1989	11169	682	114	1.02	54	7.91
Total	95734	5688	966	1.01	429	7.54

TABLE 2 : Showing the incidence of tetanus in different age groups.

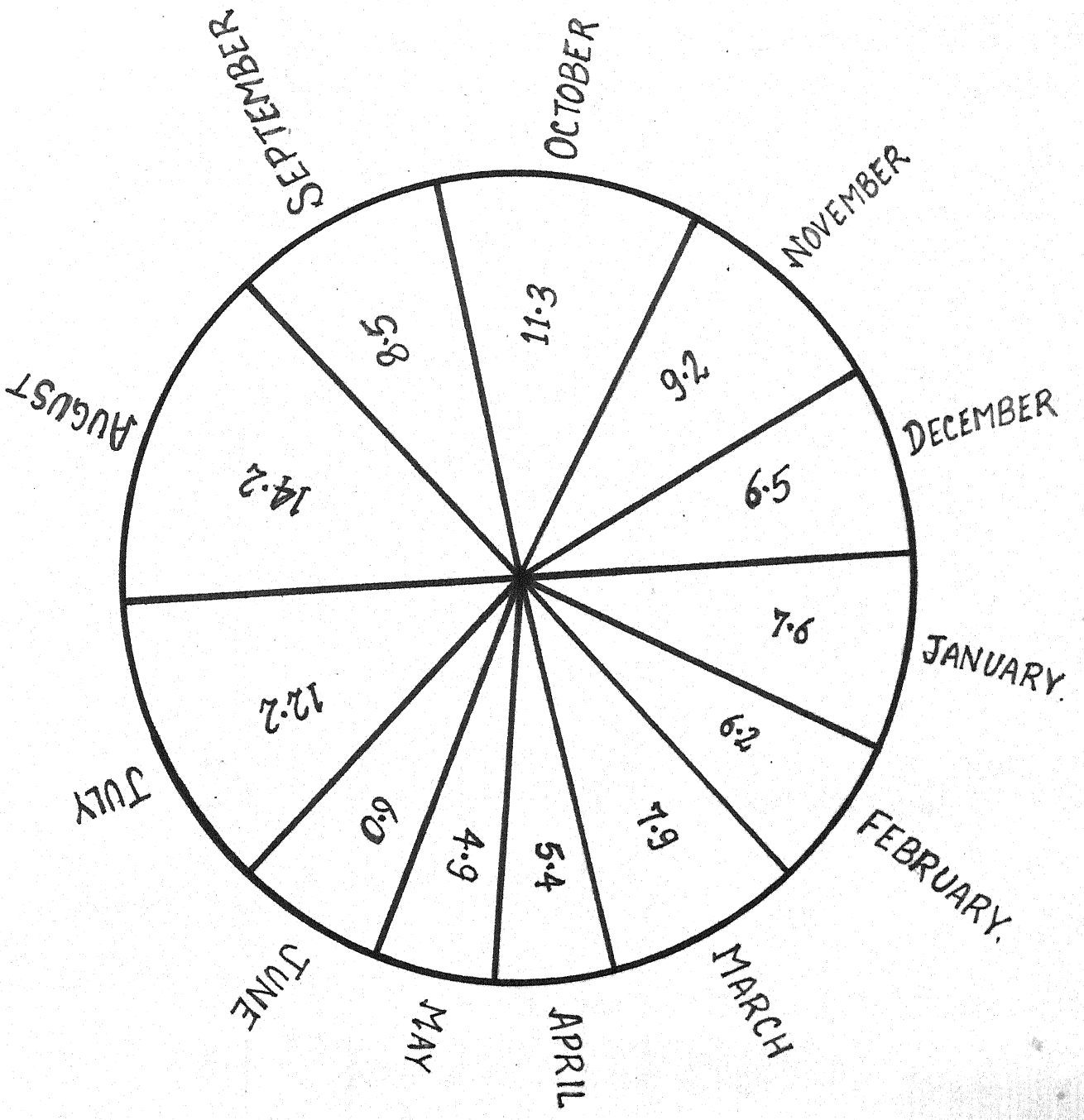
Age groups	No.of cases	Percentage
Tetanus neonatorum	309	31.98
Childhood	315	32.60
Adulthood	342	35.42
Total	966	100.00

TABLE 3 : Showing L.A.M.A. and studied cases in different age groups.

Age groups	Total No. of cases	Studied cases		LAMA cases	
		No.	%	No.	%
Neonatorum	309	239	29.22	70	22.65
Childhood	315	272	33.25	43	13.64
Aduldhood	342	307	37.53	35	10.23
Total	966	818	100.0	148	15.47

TABLE 4 : Showing the seasonal variation in tetanus cases.

Age groups	Percentage of seasonal cases		
	July-Oct. Rain	Nov.-Feb. Winter	March-June Summer
Neonatorum(239)	70.64	18.77	10.58
Childhood(272)	36.73	34.48	28.73
Aduldhood(304)	30.20	35.90	33.89
Total (818)	46.12	29.57	24.29



PIE DIAGRAM SHOWING SEASONAL VARIATION OF TETANUS CASES.

TABLE 5 : Showing incidence of tetanus and mortality according to sex.

Age groups	Total cases	Male	Female	Male: Female Ratio	Deaths	DEATHS IN				Death Ratio M : F
						Male		Female		
						No.	(%)	No.	(%)	
Neonatorum	239	195	44	4.4:1	198	159	80.30	39	19.70	4.1:1
Childhood	272	196	76	2.6:1	77	45	58.40	32	41.60	1.4:1
Adulthood	307	185	122	1.5:1	154	89	57.70	65	42.20	1.4:1
Total	818	576	242	2.4:1	429	293	68.10	136	31.70	2.1:1

TABLE 6 : Showing the incidence and mortality of tetanus according to rural/urban areas.

Age groups	Total cases	Rural Areas			Urban areas		
		No.of cases	Mortality		No.of cases	Mortality	
			No.	Percentage		No.	Percentage
Neonatorum	239	214	179	83.64	25	19	76.00
Childhood	272	250	70	28.00	22	7	31.81
Adulthood	307	280	139	49.64	27	15	55.55
Total	818	744	388		74	41	
Percentage		90.96		52.15	9.04		55.40

TABLE 7(A) : Showing the mortality in neonates in relation to method of cord cutting.

Instrument used	Cases		Mortality	
	No.	(%)	No.	(%)
Unsterilized				
Shaving blade	150	62.76	149	99.33
Knife	15	6.27	15	100.00
Sickle	8	3.34	8	100.00
Razor	7	2.92	6	85.71
Scissor	4	1.67	4	100.00
Tin foil	3	1.25	3	100.00
Sterilized shaving blade	51	21.33	13	25.49
Hospital delivery	1	0.41	-	-
Total	239	100.00	198	82.84

TABLE 7(B) : Showing childhood mortality in relation to aetiological factors.

Mode of infection	Cases		Mortality	
	No.	(%)	No.	(%)
Otorrhoea	112	41.17	27	24.10
Injury	35	12.86	13	37.14
Thorn prick	25	9.19	6	24.00
Injection	17	6.25	6	35.29
Postoperative	4	1.47	2	50.00
Post measles	8	2.94	6	75.00
Burn	6	2.20	6	100.00
Sepsis	5	1.83	5	100.00
Unknown	60	22.05	10	16.67
Total	272	100.00	77	28.30

TABLE 7(C) : Showing incidence and mortality in adult tetanus cases in relation to mode of infection.

Mode of infection	Total cases		Mortality	
	No.	(%)	No.	(%)
Postpartum and post abortal	38	12.37	25	65.78
Ear infection(Otorrhoea)	20	6.51	5	25.00
Injury	110	35.83	60	54.54
Burn	3	0.97	2	66.67
Thorn prick	11	3.58	8	72.72
Nail prick	5	1.62	3	60.00
Biopsy	1	0.32	-	-
Injection	10	3.20	4	40.00
Goat bite	1	0.32	-	-
Gun shot injury	3	0.97	1	33.33
Tongue bite	3	0.97	-	-
Tooth extraction	3	0.97	-	-
Oropharyngeal carcinoma	1	0.32	-	-
Unknown	98	31.92	46	46.93
Total	307	100.00	154	50.16

TABLE 8 : Showing case fatality rate.

Groups	Total cases	Deaths	%tage of total cases (818)	%tage of total deaths (429)	%tage of fata-lity
Neonatorum	239	198	24.20	46.15	82.84
Childhood	272	77	9.41	17.94	28.30
Adulthood	307	154	18.82	35.89	50.16
Total	818	429			52.44

TABLE 9 : Showing mortality rate according to age.

Age groups	No.of cases	%tage of total cases (818)	No.of deaths	Percentage of Total deaths (429)	Deaths in each group	Fatality rate
NEONATORUM						
0 - 4 days	7	00.86	7	1.63	3.53	100.00
5 - 10	199	24.30	172	40.10	87.00	86.40
11- 20	33	4.03	19	4.42	9.60	57.60
21 - 30	-	-	-	-	-	-
Total	239	-	198	46.15	-	82.84
CHILDHOOD (years)						
1 mo - 1 year	3	00.37	1	0.23	1.29	33.33
1 - 2	29	3.54	8	1.26	10.38	27.58
3 - 4	62	7.60	26	6.06	33.76	41.93
5 - 6	56	6.84	16	3.72	20.77	28.57
7 - 8	57	6.96	12	2.79	15.58	21.05
9 - 10	30	3.66	7	1.63	9.09	23.33
11 - 12	35	4.27	7	1.63	9.09	20.00
Total	272		77	17.94		28.30
ADULTHOOD (Years)						
13 - 20	80	9.77	43	10.02	27.90	53.75
21 - 30	107	13.08	48	11.18	31.16	44.85
31 - 40	50	6.11	24	5.59	15.58	48.00
41 - 50	38	4.64	17	3.96	11.03	44.70
51 - 60	24	2.93	17	9.96	11.03	70.80
7 60	8	0.97	5	1.16	3.24	62.50
Total	307		154	35.80		50.16
TOTAL	818	100.00	429	100.00		52.54

TABLE 10 : Showing incubation period and its relationship with mortality in tetanus cases.

Incubation period (days)	No. of cases	%tage of total cases	No. of deaths	%tage of deaths	%tage of mortality
NEONATORUM					
0 - 7	182	76.15	159	80.30	87.36
8 - 14	53	22.17	39	19.69	73.58
15 - 21	3	1.25	-	-	-
7 21	1	0.41	-	-	-
Total	239	100.00	198	100.00	82.84
CHILDHOOD					
0 - 7	46	16.91	17	22.07	36.95
8 - 14	21	7.72	3	3.89	14.28
15 - 21	13	4.77	2	2.59	15.38
7 21	40	14.70	2	2.59	5.00
Unknown	152	55.88	53	68.83	34.86
Total	272	100.00	77	100.00	28.30
ADULTHOOD					
0 - 7	96	31.27	63	40.90	65.62
8 - 14	65	21.17	29	18.83	44.61
15 - 21	17	5.53	4	2.59	23.52
7 21	29	9.44	9	5.84	31.03
Unknown	100	32.57	49	31.81	49.00
Total	307	100.00	154	100.00	50.16
TOTAL TETANUS CASES					
0 - 7	324	39.60	239	55.71	73.76
8 - 14	139	16.99	71	16.55	51.07
15 - 21	33	4.03	6	1.39	18.18
7 21	69	8.43	11	2.56	15.94
Unknown	253	30.92	102	23.77	40.31
TOTAL	818	100.00	429	100.00	52.44

TABLE 11 : Showing period of onset and its relationship with mortality in tetanus cases.

Period of onset (hours)	No.of cases	%tage of total cases	No. of deaths	%tage of deaths	%tage of mortality
NEONATORUM					
∠ 24	180	75.31	168	84.84	93.33
25 - 48	37	15.48	28	14.14	75.67
49 - 72	1	0.41	-	-	-
73 - 96	1	0.41	-	-	-
7 96	7	2.92	2	1.01	28.57
No spasm	13	5.43	-	-	-
Total	239	100.00	198	100.00	82.84
CHILDHOOD					
∠ 24	101	37.13	56	72.72	55.44
25 - 48	53	19.48	16	20.77	30.18
49 - 72	28	10.29	2	2.59	7.14
73 - 96	20	7.35	1	1.29	5.00
7 96	20	7.35	1	1.29	5.00
No spasm	50	18.38	1	1.29	2.00
Total	272	100.00	77	100.00	28.30
ADULTHOOD					
∠ 24	110	35.83	94	61.03	85.30
25 - 48	57	18.56	35	22.72	61.40
49 - 72	24	7.81	9	5.84	37.50
73 - 96	11	3.58	4	2.59	36.36
7 96	27	8.79	5	3.24	18.51
No spasm	78	25.40	7	4.54	8.97
Total	307	100.00	154	100.00	50.16
TOTAL TETANUS CASES					
∠ 24	391	47.79	318	74.12	81.32
25 - 48	147	17.97	79	18.41	53.74
49 - 72	53	6.47	11	2.56	20.75
73 - 96	32	3.91	5	1.16	15.62
7 96	54	6.60	8	1.86	14.81
No spasm	141	17.23	8	1.86	5.67
Total	818	100.00	429	100.00	52.44

TABLE 12 : Showing prognosis in relation to duration of symptoms before admission.

Duration of symptoms before admission (Days)	No. of cases	Deaths	Percentage of Mortality
Upto 1 day	286	210	73.42
2	208	120	57.69
3	125	54	43.20
4	67	20	29.85
5	54	13	24.07
6	40	5	12.50
7	18	3	16.67
8	9	2	22.22
7 8	11	2	18.18
Total	818	429	52.44

TABLE 13 : Showing mortality in relation to grades of severity of tetanus.

Grades	Total cases	Deaths	%tage of mortality
NEONATORUM			
I	4	1	25.00
II	13	5	38.46
III	19	13	68.42
IV	95	83	87.36
V	97	85	87.62
Unknown	11	11	100.00
Total	239	198	82.84
CHILDHOOD			
I	16	-	-
II	61	7	11.47
III	87	26	29.88
IV	79	28	35.44
V	27	14	51.85
Unknown	2	2	100.00
Total	272	77	28.30
ADULTHOOD			
I	15	-	-
II	72	25	34.72
III	101	50	49.50
IV	69	43	62.31
V	47	33	70.21
Unknown	3	3	100.00
Total	307	154	50.16

TABLE 14 : Showing mortality in relation to days after hospital admission.

Groups	Total deaths	Number of cases died on days										7/10
		1	2	3	4	5	6	7	8	9	10	
Neonatorum	198	113	37	18	9	3	3	3	3	1	3	5
(%)		57.01	18.68	9.09	4.54	1.51	1.51	1.51	1.51	0.50	1.51	2.52
Childhood	77	28	23	11	5	3	2	-	2	-	1	2
(%)		36.36	29.87	14.28	6.49	3.89	2.59	-	2.59	-	1.29	2.59
Adulthood	154	36	37	28	16	10	6	1	5	-	2	13
(%)		23.37	24.02	18.18	10.38	6.49	3.89	0.64	3.24	-	1.29	8.44
Total	429	177	97	57	30	16	11	4	10	1	6	20
(%)		41.25	22.61	13.28	6.99	3.72	2.56	0.93	2.33	0.23	1.39	4.66

TABLE 15 : Shwoing mortality in different grades of tetanus neonatorum in relation to various forms of treatment.

Grade of tetanus	Total cases	A.T.S.			Intrathecal TIG			Intramuscular TIG			No treatment		
		No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage
I	4	2	1	50.00	2	-	-	-	-	-	-	-	-
II	13	3	2	66.67	6	-	-	2	1	50.00	2	2	100.0
III	19	7	6	85.71	5	1	20.00	5	4	80.00	2	2	100.0
IV	95	33	33	100.00	44	33	75.00	10	9	90.00	8	8	100.0
V	97	8	8	100.00	71	59	83.10	4	4	100.0	14	14	100.0
Unknown	11	9	9	100.00	-	-	-	-	-	-	2	2	100.0
Total	239	62	59	95.16	128	93	72.10	21	18	85.71	28	28	100.0

TABLE 16 : Showing the mortality in different grades of childhood tetanus in relation to various modes of treatment.

Grades of tetanus	Total Cases	A.T.S.			Intrathecal TIG			Intramuscular TIG			No treatment		
		No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage
I	16	7	-	-	1	-	-	6	-	-	2	-	-
II	61	25	4	16.00	25	-	-	8	1	12.50	3	2	66.67
III	87	28	15	53.57	45	5	11.11	12	4	33.33	2	2	100.0
IV	79	5	5	100.0	68	18	26.50	4	3	75.00	2	2	100.0
V	27	6	6	100.0	21	8	38.10	-	-	-	-	-	-
Unknown	2	2	2	100.0	-	-	-	-	-	-	-	-	-
Total	272	73	32	43.83	160	31	20.00	30	8	26.60	9	6	66.67

TABLE 17 : Showing the mortality in different grades of adult tetanus in relation to various modes of treatment.

Grade of tetanus	Total cases	A.T.S.			Intrathecal TIG			Intramuscular TIG			No treatment		
		No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage	No.of cases	Deaths	Percentage
I	15	7	-	-	5	-	-	-	-	-	3	-	-
II	72	23	12	52.00	28	3	10.71	14	5	35.71	7	5	71.00
III	101	26	21	80.76	48	12	25.00	23	13	56.52	4	4	100.0
IV	69	6	6	100.0	50	25	50.00	10	9	90.00	3	3	100.0
V	47	6	6	100.0	34	20	58.00	5	5	100.0	2	2	100.0
Unknown	3	1	1	100.0	-	-	-	1-	1	100.0	1	1	100.0
Total	307	69	46	66.70	165	60	36.40	53	33	62.30	20	15	75.00

TABLE 18 : Showing the mortality in relation to doses of human TIG.

Dose of TIG	Neonatorum			Childhood			Adulthood		
	No.of cases	No.of deaths	Percentage	No.of cases	No. of deaths	Percentage	No.of cases	No. of deaths	Percentage
250 IU	71	60	84.50	43	11	25.58	25	16	64.00
500 IU	66	49	74.24	130	25	19.23	135	59	43.70
1000 IU or more	3	2	66.67	17	3	17.64	58	18	31.03
Total	140	111		190	39		218	93	

TABLE 19 : Showing mortality in relation to day of administration of human antitetanus immunoglobulins.

Day of administration	Neonates			Children			Adults		
	No.of cases	No. of deaths	Percentage	No.of cases	No. of deaths	Percentage	No.of cases	No. of deaths	Percentage
1st	120	90	77.50	168	27	16.07	200	78	39.00
2nd	14	12	85.71	15	5	33.33	13	10	61.53
3rd or beyond	6	6	100.00	7	7	100.00	5	5	100.00
Total	140	111		190	39		218	93	

OBSERVATIONS

1. HOSPITAL INCIDENCE OF TETANUS

During 1985 January to 1989 June, a total of 95734 patients were admitted at MLB Medical College, Hospital, Jhansi. Out of these total tetanus cases were 966 thus they constituted about 1.01 per cent of total hospital admission. During this period total hospital deaths were 5688, out of which tetanus deaths were 429 making 7.54% of total hospital deaths (Table 1).

2. INCIDENCE OF TETANUS IN DIFFERENT AGE GROUPS

Out of total 966 cases of tetanus admitted during Jan., 1985 to June, 1989, 309 cases (31.98%) were of tetanus neonatorum, 315(32.60%) cases were of childhood tetanus and rest 342 (35.42%) were of adult tetanus (Table 2).

3. TOTAL STUDY

Out of 309 cases of tetanus neonatorum 70(22.65%) patients left against medical advice(LAMA) thus 239 cases could be studied. Out of 315 cases of childhood tetanus, 43(13.64%) patients left against medical advice, thus 272 patients could be studied.

Out of 342 cases of adult tetanus, 35(10.23%) cases left against medical advice, thus 307 patients could be studied. Out of total 966 cases of tetanus

admitted during the year from Jan., 1985 to June, 1989, 148(15.47%) cases left against medical advice so 818 cases could be studied (Table 3).

4. SEASONAL VARIATIONS IN TETANUS

Incidence of childhood and neonatal tetanus were higher in rainy season i.e. July-October, while adulthood tetanus showed higher incidence during winter season. Nearly 46.12% of all tetanus admissions were during rainy seasons(July-Oct.), 70.64% cases of neonatorum tetanus came in rainy season (Table 4).

5. INCIDENCE OF TETANUS IN DIFFERENT SEX GROUPS

Out of 818 cases of tetanus studied, 576 cases were male and rest 242 cases were female, so with male:female ratio of 2.4:1. In tetanus neonatorum male:female ratio of 2.4:1, in childhood tetanus the ratio was 2.6:1 and in adult tetanus it was 1.5:1 (Table 5).

6. INCIDENCE OF TETANUS IN RURAL/URBAN AREAS

Out of 818 cases, 744 (90.96%) cases belonged to rural area and remaining 74(9.04%) cases belonged to urban area (Table 6).

7. AETIOLOGICAL FACTORS IN THE CAUSATION OF TETANUS

Out of 818 cases of tetanus studied 239 cases were of tetanus neonatorum, in which aetiolo-

gical factor was cord cutting by unsterilized objects like shaving blades, knife, sickle, razor, scissor and tin foil. In most of the cases cord was dressed by contaminated material like ash, cowdung, foil etc.

In childhood tetanus (272 cases) otitis media was the important factor responsible for tetanus. It was responsible for 41.17% cases of childhood tetanus while in adult tetanus it was responsible for only 6.51% cases.

Injury was responsible for 12.86% cases of childhood tetanus and 35.83% cases of adulthood tetanus.

Postpartum and post abortion infection was responsible for 12.37% cases of adult tetanus. In 22.05% cases of childhood tetanus and 31.92% cases of adult tetanus no specific cause could be searched.

Other factors responsible for causation of tetanus were thorn prick, nail prick, infection by unsterilized needle and syringe, burn, post measles, post operative infection, gun shot injury, tooth extraction etc. (Table 7A, 7B and 7C).

8. FATALITY RATE

Out of 818 cases studied 429 cases expired making the case fatality rate of 52.44%. Individually in tetanus neonatorum case fatality rate was 82.84%, in childhood tetanus it was 28.30% and in adult tetanus it was 50.16% (Table 8).

9. MORTALITY ACCORDING TO AGE GROUPS

In tetanus neonatorum out of 198 deaths, 3.53% deaths occurred in 0-4 days old neonates with 100% fatality rate and 87% deaths occurred in 5-10 days old neonates with fatality rate of 86.40%.

In childhood tetanus out of 77 deaths 33.76% deaths occurred in 3-4 years of age and 20.77% in 3-6 years of age group. Maximum fatality rate was (41.93%) found in children between 3-4 years of age followed by 33.33% in children below 1 year of age. Minimum fatality was found in children between 10-12 years of age (Table 9).

In adults tetanus out of total 154 deaths 31% deaths occurred in 20-30 years of age group with fatality rate of 44.85%, fatality rate declined to 44.70% in 40-50 years of age but it rises and became 70-80% in cases which are more than 50 years old (Table 9).

10. INCUBATION PERIOD OF TETANUS

Incubation period could be known correctly in those cases in which a definite period of occurrence of causative factor could be known. Incubation period in tetanus neonatorum was considered to be from the date of birth. It was found to be 46.15% in cases between 0-7 days of age. It was observed that mortality was higher (87.36%) with a short incubation period.

In childhood tetanus incubation period of more than 21 days was found in 14.7% cases and was unknown in 55.88% cases. In childhood tetanus mortality was higher 36.95% with shorter incubation period of 0-7 days.

In adult tetanus incubation period between 0-7 days was found in 31-27% cases with fatality rate of 65.62% it was unknown in 32.57% cases(Table 10).

11. PERIOD OF ONSET IN TETANUS

In neonatorum tetanus period of onset was leas than 24 hours in 75.31% cases and between 25-48 hours in 15.48% cases. Mortality was higher in 93.33% with a short period of onset less than 24 hours. In childhood tetanus period of onset was less than 24 hour in 37.13% cases with mortality of 55.44% and 25-48hours in 19.48% cases with a mortality of 30.18% (Table 11).

In adult tetanus period of onset was less than 24 hours in 35.83% cases with mortality rate of 85.30% (Table 11).

12. MORTALITY ACCORDING TO SEX

In tetanus neonatorum male, female death ratio was 4.1:1. In childhood and adulthood tetanus it was 1.4:1 for each group. An average male:female death ratio was 2.1:1, which was similar to male, female incidence ratio of 2.4:1 (Table 5).

13. MORTALITY ACCORDING TO AETIOLOGY

Mortality rate due to tetanus neonatorum is 82.84%. Mortality was lower in cases where sterilized blade was used for cutting the cord. In childhood tetanus cases 24.1% of total deaths occurred in cases having tetanus following otitis media. Mortality was 100% in cases having tetanus following burn and sepsis.

In the adult tetanus out of total 154 deaths, 25 (65.78%), occurred in cases having tetanus following post partum and post abortion with fatality rate of 65.68%. Eight deaths occurred in patients having thorn prick with fatality rate of 72.72% in cases having tetanus following injury fatality was 54.54% (Table 7A, 7B and 7C).

14. MORTALITY IN RELATION TO PERIOD OF ONSET

Mortality rate was higher in all the groups having period of onset less than 24 hours. Total mortality rate was 81.32% with period of onset less than 24 hours. It was 53.74% in patients having period of onset between 25-48 hours. It shows that mortality decreases as the period of onset increases (Table 11).

15. MORTALITY IN RELATION TO INCUBATION PERIOD

Mortality rate decreases as incubation period increases. Fatality rate was 78.76% in allthe tetanus patients having incubation period between 0-7 days and 15.94% in patients having incubation

period of more than 21 days (Table 10).

16. MORTALITY IN RELATION TO SEVERITY OF DISEASE

Mortality was directly related with severity of disease. In tetanus neonatorum mortality was 67.62% in grade V cases and 25% in grade I cases. In childhood tetanus mortality was 51.85% in grade V as compared to 11.47% in grade I. In adult tetanus cases mortality was 70.21% in grade V as compared to 0 in grade I (Table 13).

17. MORTALITY IN RELATION TO DAYS AFTER HOSPITAL ADMISSION

Out of total 429 deaths, 174 cases(41.25%) died within 24 hours of hospital admission. This rate decreased to 1(0.23%) on 9th day, after 10th day the mortality was 4.66%. These cases died due to respiratory infections (Table 14).

18. MORTALITY IN RELATION TO DURATION OF SYMPTOMS BEFORE ADMISSION

Mortality was higher (73.42%) in patients having duration of symptoms 10 days before admission. Mortality was low (12.5%) in patients having duration of symptoms less than 6 days before admission(Table 12).

19. EFFECTIVENESS OF HUMAN IMMUNOGLOBULINS IN THE ESTABLISHED CASES OF TETANUS

Mortality was lower in patient treated with intrathecal administration of human antitetanus globulins :

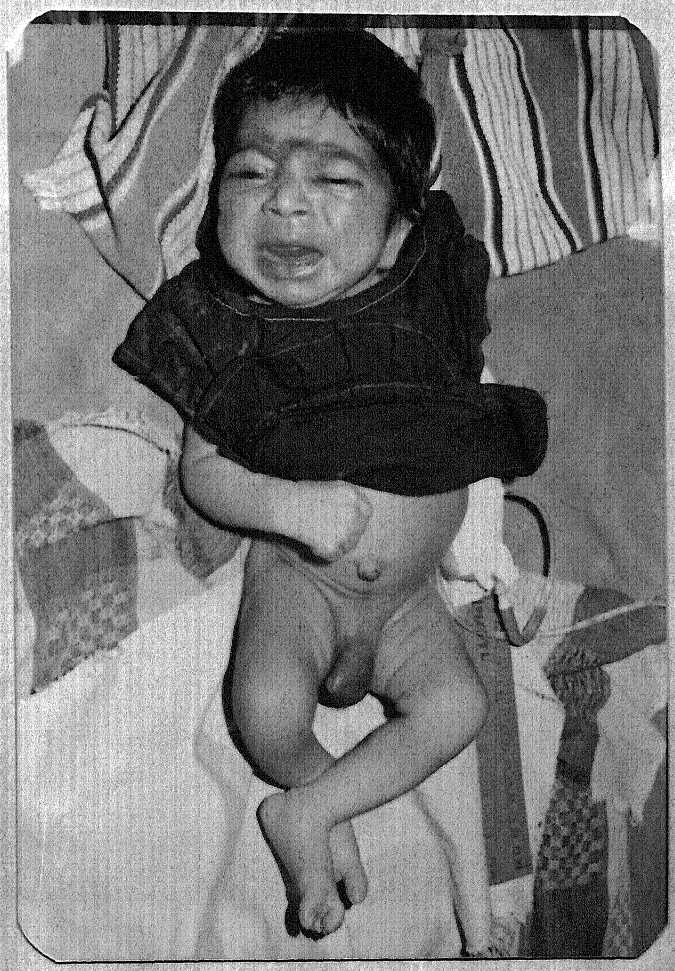
- In the cases of tetanus neonatorum mortality was 72.09% in intrathecal groups, 85.71% in patients treated with intramuscular human TIG. In the group treated with ATS mortality was 95.16% (Table 15).
- In the cases of childhood tetanus mortality was 20% in the group treated with intrathecal administration of human TIG. Mortality was 26.60% in patients treated with intramuscular human TIG. Mortality was 43.83% in group treated with ATS. (Table 16).
- In adult tetanus cases mortality was higher (66.67%) in cases treated with ATS. Mortality was lower (36.36%) in the groups treated with intrathecal administration of human TIG(Table 17).

20. RELATION OF MORTALITY WITH DOSES OF HUMAN ANTITETANUS GLOBULINS

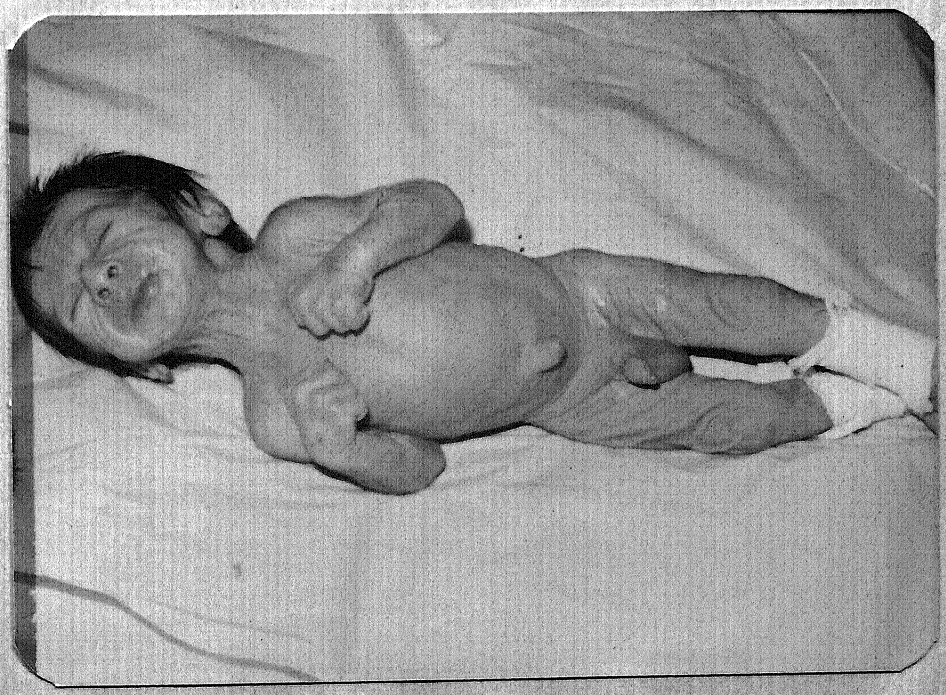
It was observed that mortality was lower with the higher doses of human antitetanus globulin In the tetanus neonatorum mortality was 84.50% with 250 IU of human TIG while it was 66.67% with the use of 1000 I.U. or more TIG (Table 18).

21. MORTALITY IN RELATION TO DAY OF ADMINISTRATION OF HUMAN ANTITETANUS IMMUNOGLOBULINS

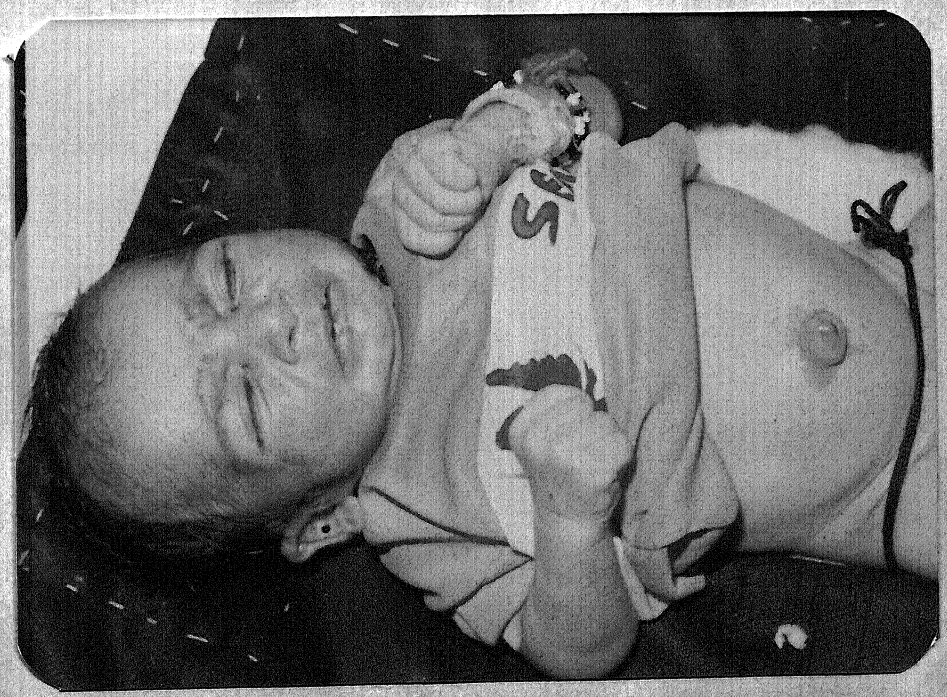
From the table 19 it can be seen that mortality was lowest in all the groups of tetanus patients when the human TIG were administered on the first day of admission. Mortality was highest (100%) in all the groups when TIG were administered on or beyond 3rd day of admission.



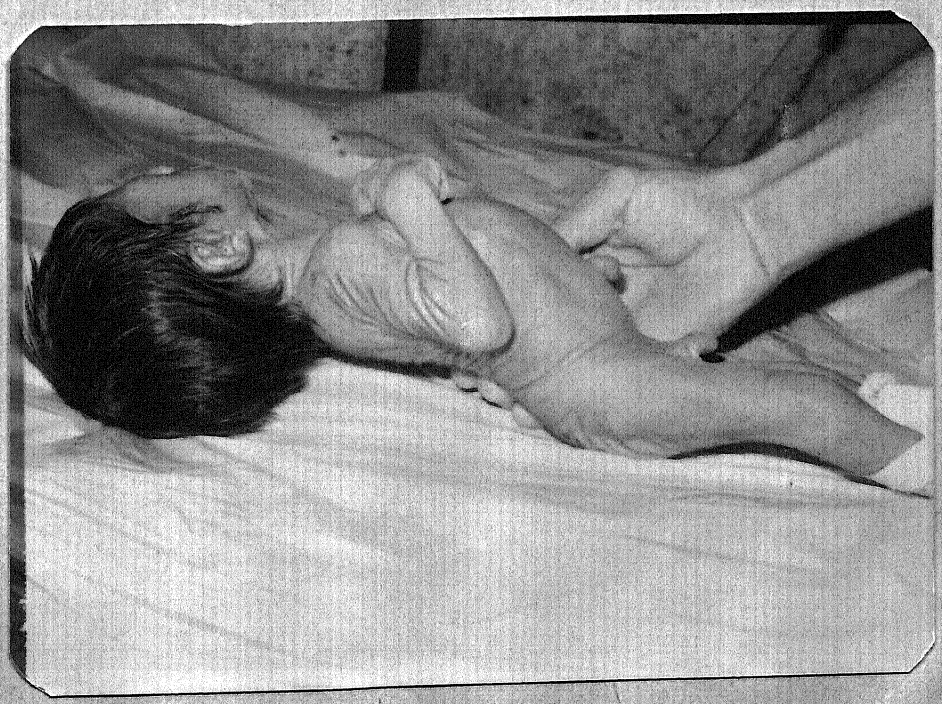
Photograph 1 : Showing a case of tetanus neonatorum who presented with excessive cry.



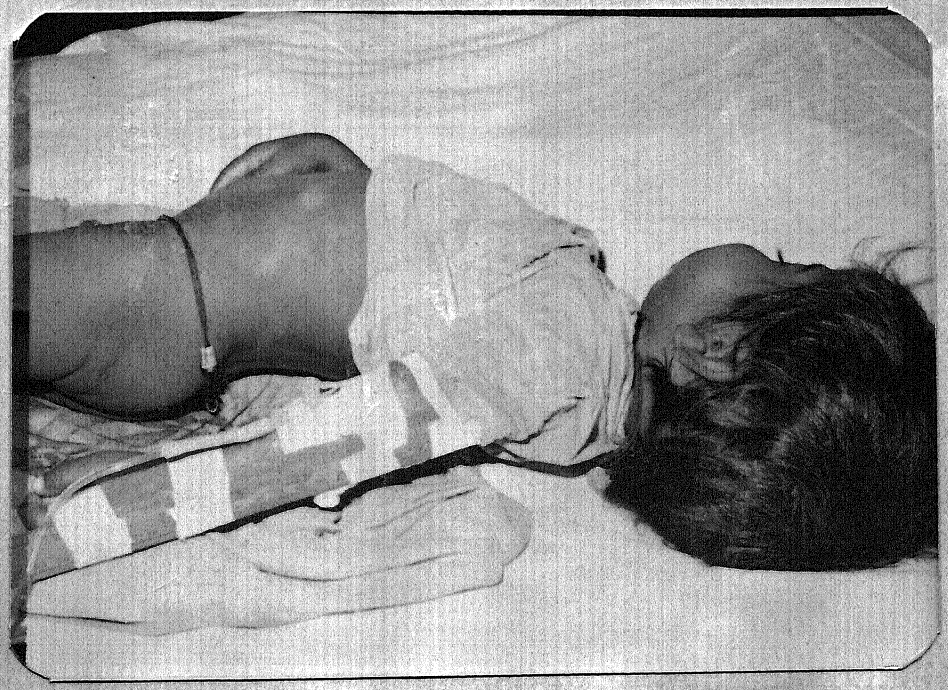
Photograph 2 : Showing a case of tetanus neonates during spasm.



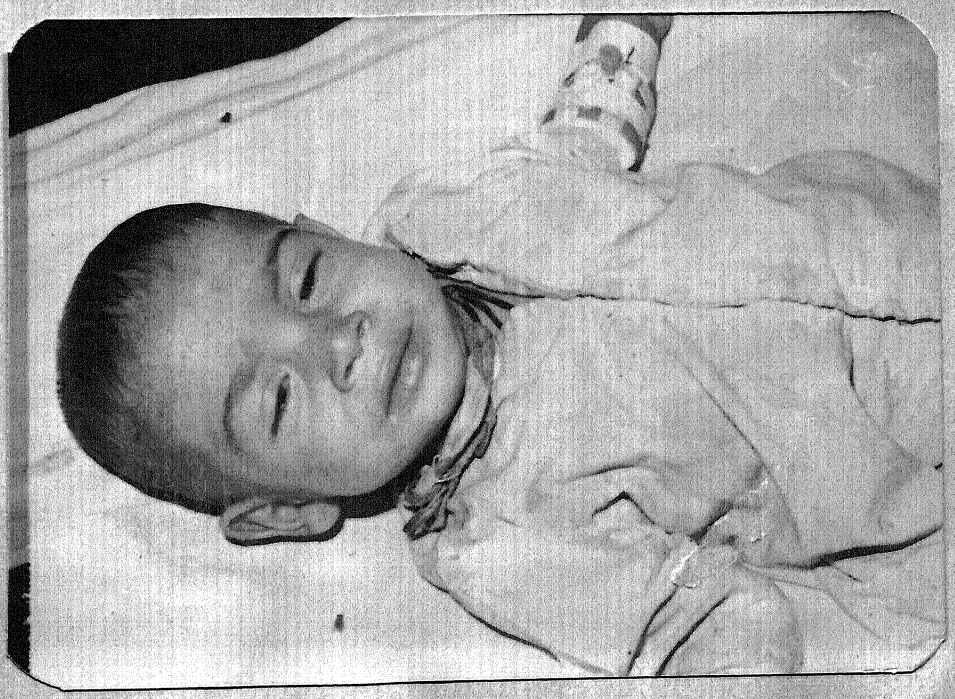
Photograph 3 : Showing gross umbilical sepsis in a case of tetanus neonatorum.



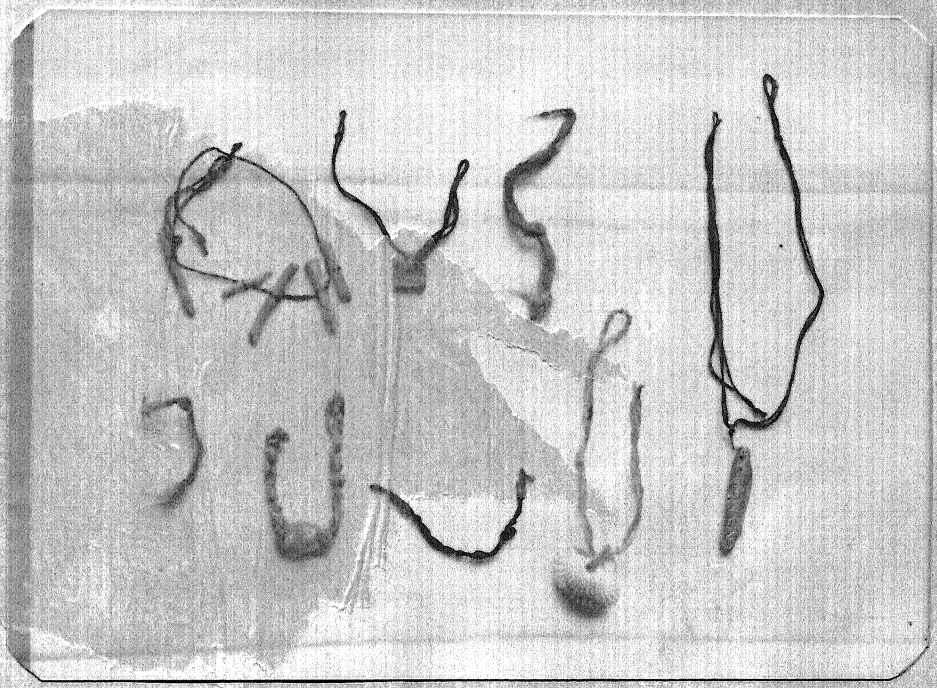
Photograph 4 : Showing a case of tetanus neonatorum with opisthotonous.



Photograph 5 : Showing a case of childhood tetanus with opisthotonous.



Photograph 6 : Showing a case of childhood tetanus during recovery phase.



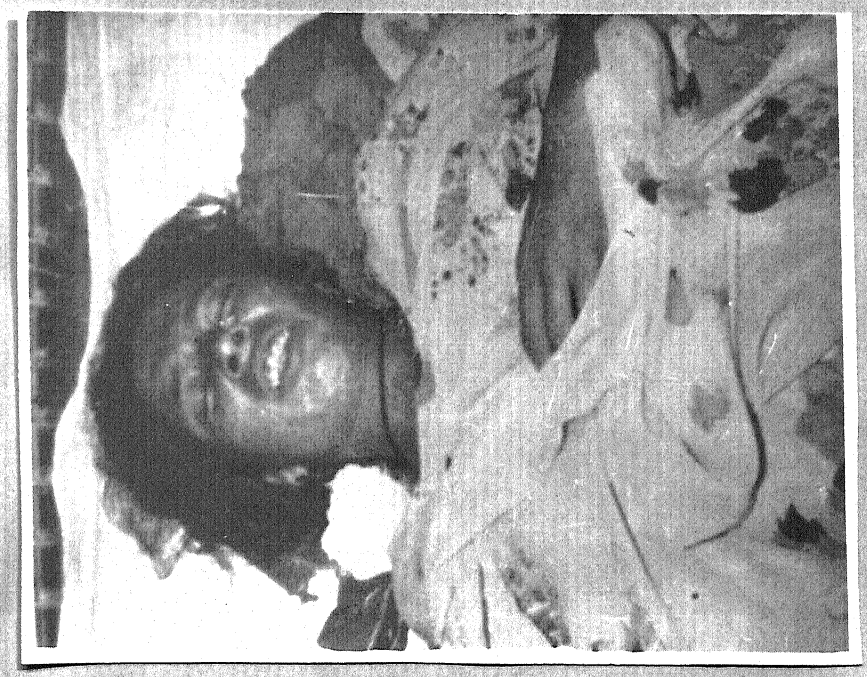
Photograph 7 : Showing Amulets mode up of different materials used in villages :

Upper row : Left to right :

- Wooden Pieces, Tabiz, Horse hairs.

Lower row : Left to right :

- human hairs, old dhoti cloth, cotton thread, kauri, small knife.



Photograph 8 : Showing a case of postpartum tetanus with characteristic facies.

DISCUSSION

DISCUSSION

Tetanus is an infection which occurs in most countries throughout the world. The tetanus is still widely prevalent in India. The disease carried a high mortality. The treatment of tetanus has been mainly symptomatic. Although number of drugs have been used to achieve the symptomatic control but no drug satisfies the criterion of an ideal drug. In the recent years human antitetanus globulins have been available for the treatment of this disease but its role is yet to be determined and mode of administration and doses need standardisation.

In the present study it is observed that tetanus comprises on average it 1.0% of total hospital admissions annually during 1985 to 1986. Srivastava and Chattarjee (1961) have reported 0.6% and Laha and Vaishya (1965) have reported 4.8% cases of tetanus out of total hospital admissions. Tetanus deaths in the present study accounted for an average 7.43% of total hospital deaths. Vaishnava et al (1966) reported 16% of total hospital deaths due to tetanus.

In the present study incidence of tetanus neonatorum was 29.22%. Bhatt et al (1979) have reported an overall incidence of 14.3% of tetanus neonatorum. Suri(1967) reported 26.8% overall incidence of tetanus neonatorum. Childhood tetanus constituted 33.25% of

total tetanus cases. Athavale et al(1974) reported in their series an incidence of 39% of total tetanus cases due to childhood tetanus. Adult tetanus contributed to 37.53% of total tetanus cases. Gorden et al (1961) reported a very high incidence of tetanus in Punjab, it was 90.4% per 1,00,000 cases per year. Adults are more active physically which makes them more prone to injuries and infections so there was a high incidence of tetanus in this age group.

A higher incidence of tetanus neonatorum was found in rainy reason (July - October) in our study. An increased birth rate in this season may be the possible reason for this (Mazumdar and Chakraborty, 1974). Bhatt et al (1979) also noted a high incidence of tetanus neonatorum in rainy season (June-Oct.). Vaishnava et al (1965) also noted high incidence of childhood tetanus during rainy season. In the present study peak incidence of childhood tetanus was found in rainy season(July-Oct.)

In our study the over all incidence of tetanus was higher in rainy season. Gupta et al (1977) reported a higher incidence of tetanus during rainy season. Vakil et al (1964) found no significant seasonal variation in tetanus cases.

The overall male : female ratio in the present study was 2.4 : 1. Mathur (1980) reported a male : female ratio of 5.4:1 in tetanus. Kacharevic (1952)

suggested that males were more sensitive to tetanus toxins as compared to females and hence a higher male preponderance. In our study male : female ratio in tetanus neonatorum was 4.4 : 1. Athavale (1974) reported a male : female ratio in tetanus neonatorum as 1.4 : 1. Male:female ratio among childhood tetanus was 2.6:1. Athavale (1974) reported a male:female ratio of 1.6:1. in childhood tetanus cases. The significant difference in the male:female ratio in tetanus neonatorum in our study may be due to the reason that the female infant is not given proper attention in villages due to dowry stigma attached with females. So most of the female babies are not brought to hospital. To save life of a male infant more attention is paid to him and various types of foreign materials are applied over the cord and greater number of male infants are also admitted in the hospital. Male:female ratio in adulthood tetanus was 1.5:1 in our study. Modi (1965) reported a higher incidence of tetanus in males in all the age groups. Denchev (1962) also suggested that males are more sensitive to tetanus toxin. Jolly et al (1974) reported the overal male:female ratio of 1.9:1 in Punjab.

In the present study rural areas contributed to about 90.96% of total cases and urban areas contributed 9.04% cases. Higher incidence of tetanus in rural areas has been reported by various other authors. Patients

drawn from rural areas were mostly labourers and farmers who are more engaged in manual work and were more exposed to clostridium tetani infection from soil. On the other hand because of lack of proper medical care and facilities in rural areas, rural people do not receive proper treatment of wounds, pricks and infections. They try home made medicines which are mostly contaminated. Illiteracy and wrong belief that cowdung is the best antiseptic to to applied to the wound and cord, is also an important factor.

Deliveries by untrained daies or elderly lady of house and use of unsterilized material for cutting the umbilical cord and dressing by contaminated substances (oil, mustard, ash and cowdung) all made the neonates more susceptible to tetanus. In our study 99.6% deliveries were home deliveries. Bottle and Punjabi (1964) observed 100% home deliveries in neonatal tetanus. In our study instrument which was commonly used for cutting the cord was unsterilized shaving blade (62.76%). In study conducted by Athavale (1974) the instrument which was commonly used for cutting the cord was unsterilized blade (21.2%).

In our study otorrhoea was the commonest aetiological factor in children (41.17%) followed by injury (12.86%). In 22.05% cases cause could not be determined. Athavale (1974) in a study found that injury was the aetiological factor in 38% children and otorrhoea in

35.8% cases. Athavale (1974) could not find aetiological factor in 20.7% cases of childhood tetanus. Wesley et al (1987) noted that tetanus was more common in bare footed children who had no obvious injury.

In our study injury was the commonest aetiological factor in the causation of adulthood tetanus (35.83%). Post partum and post abortal infection contributed to 12.37% of total adult cases and in 31.92% cases the aetiological factor could not be determined. According to Jolly et al(1974) injury was been noted as an aetiological factor in most of the adult tetanus cases (38%) and the cause could not be detected in significantly large number of cases (35.5%). According to the observation of Srivastava and Chatterji (1961). Shah et al (1962) and Bhatt (1962) puerperal tetanus contributes to 10 to 12.7% of all cases. A high incidence of postpartum and post abortal tetanus is due to faulty and unhygenic practices of deliveries, poor post partum care and unhygenically conducted illegal abortions. Post partum uterus provides a good anaerobic environment for clostridium and this could be the possible explanation for puerperal tetanus.

Overall case fatality rate in present study was 52.44% in all the cases of tetanus with tetanus neonatorum having maximum fatality rate (82.84%) and fatality in childhood and adult tetanus was 28.3% and

50.16% respectively. Jolly et al (1974) have reported overall case fatality rate of 41%. Bytchenko (1966) has quoted overall case fatality rate of tetanus during 1950-51 between 26.5 to 76.1% in Japan and Phillipines respectively. Bhatt and Anwikar (1962) have reported case fatality rate due to tetanus in India as 45.9%. Athavale et al (1974) have reported case fatality rate of tetanus neonatorum as 76.4%.

Bytchenko reported case fatality rate of tetanus neonatorum in Japan as 57.1% and Indonesia as 77.3%. Bhatt and Anwikar (1962) reported case fatality rate due to tetanus neonatorum as 85.9%. Patel and Mehra (1960) reported case fatality rate due to tetanus neonatorum as 86.4%. Bhandari et al (1973) reported the case fatality rate 62%. Athavale et al (1974) reported case fatality rate due to childhood tetanus as 27.8%. Jolly et al (1974) reported a mortality of 37.69% due to tetanus in children. Pathak et al (1973)reported 87.8% mortality in neonatal tetanus.

In our study regarding age, mortality was higher in neonates upto the age of 10 days(86.4%). Athavale (1974) reported that mortality was quite high i.e. above 80% upto the age of 8 days. In childhood tetanus cases mortality was higher in the age group 3-4 years (41.93%) and in adults between 51-60 years of age(70-80%). Athavale (1974) reported that mortality does not differ in different age groups in children. Jolly et al (1974)

observed highest mortality in adulthood tetanus (76.47%) in the age group of 41-50 years and 50% mortality in the age group of 51-60.

In the present study overall male:female death ratio was 2.1:1, which was similar to that of 2.4:1. Indira et al (1975) found lower mortality in males than females (0.8:1). Suri (1967) found that tetanus mortality in the two sexes does not differ musch. Modi(1965) reported higher mortality in males in all the ages groups than females. Jolly et al (1974) reported male:female mortality ratio of 1.1:1. The high mortality in neonates can be explained by the fact that on entry of tetanus spores in infant's umbilical cord, the exotoxins released are quantitatively same as in adults (Khanna et al,1985). In our study male:female mortality ratio in neonatal group was 4.1:1, which was similar to the male:female incidence ratio of 4.4:1 in this group. Male:Female mortality ratio in childhood tetanus was 1.4:1 and in adulthood tetanus it was 1.4:1. Suri (1974), Newel(1966) and Martin-Bouyer (1966) reported that mortality did not differ significantly in the two sexes in all the age groups.

In our study mortality was higher in urban areas than rural areas in all the age groups. The overall urban mortality was 55.4% as compared to 52.15% in rural areas. According to Sokhey et al (1983) the mortality due to tetanus ranged from 0-68.7% in urban

areas and 16.4% to 72.5% in rural areas. Stanfield et al (1973) have also reported a significant rural/urban difference in tetanus mortality. The possible explanation for higher mortality in urban areas could be that because of lack of proper medical care and facilities in rural areas the patients are rushed to hospital as soon as symptoms appear with immediate treatment and lower mortality seen in rural tetanus patients(52.15%). On the other hand urban patients are admitted in hospital in advanced stage of the disease due to wastage of time by local unqualified persons leading to high mortality.

In our study it was observed that mortality was higher in those neonates whose cord was cut by unsterilized instruments like knife (100% mortality) sickle (100% mortality) shaving blade (99.33%) mortality, Scissor (100%). Mortality was lower in cases where cord was cut by sterilized instrument (25.49%). Athavale et al (1974) reported that mortality was 76% with scissor, 78% with unsterilized blade and 94.1% with sickle.

In our study higher mortality was seen in childhood tetanus cases following Burn (100%), sepsis (100%), Measles (75%). Mortality was 24.1% in cases following otorrhoea and 24% in cases receiving thorn prick. Athavale et al (1974) reported childhood tetanus mortality of 66.6% following burn, sepsis-22.2%, and zero in cases following measles. Otorrhoea was responsible for 15.1% mortality.

In our study post partum and post abortal tetanus has a high mortality (65.78%). Shah et al(1962) found 59% mortality in post partum and post abortal cases.

A low mortality in childhood tetanus cases indicates that children could withstand the disease better. La force (1969) pointed out high case fatality rates in tetanus in the extremes of age group.

In the present study it was observed that mortality was hihger in cases where incubation period was short. In tetanus neonatorum mortality was 87.36% with incubation period less than 7 days. and zero with incubation period more than 21 days. In childhood tetanus cases mortality was 36.95% with incubation period less than 7 days and 05% with more than 21 days's incubation period. In adulthood tetanus cases mortality was 65.62% with incubation period of less than 7 days and 31.03% with more than 21 days incubation period. Athavale et al (1974) reported neonatal mortality of 82% with incubation period upto 7 days and 25% with incubation period of more than 25 days. Athavale et al (1974) reported childhood mortality of 37% with incubation period less than 7 days and 12.9% with incubation period more than 21 days. Jofferi et al (1966) and Beaty et al (1980) noted high mortality with incubation period less than 7 days. Jolly et al (1974) and Vaishnava et al (1966) have reported similar observations. Calvin

and Goldbergh (1977) reported the relation of mortality with incubation period as follows :

1 to 5 days - 84%; 5 -10 days - 83%, ten to 14 days - 37%; 2 to 3 weeks - 25%, 3 to 4 weeks - 33% and more than 4 weeks - 10%. In Patel (1963) series mortality in relation to incubation period was as follows : 1 to 7 days - 52.2%; 8 to 14 days - 34.7%; 15 to 21 days - 28.5% and more than 21 days - 26.6% and unknown cases - 32.6%.

In the present study it was observed that mortality was higher in total tetanus cases (81.32%) when period of onset was less than 24 hours, mortality was lowest in absence of spasms (5.67%). Jolly et al (1974) have reported mortality of 78.2% in total tetanus cases when period of onset was less than 24 hours. Cole (1940) found that a short period of onset was associated with worse prognosis. Similar observations have been noted by Athavale et al (1974), Jolly et al (1974), Bhatt et al (1962); Pathak et al (1973) and Patel et al (1963).

In our study mortality in tetanus neonatorum was 93.33% when period of onset was less than 24 hours and there was low mortality when even the mildest sign was not present. Athavale et al (1974) have reported 84.8% mortality with period of onset less than 24 hours and 10% when period of onset was absent. In our study childhood mortality was 55.44% when period of onset was

less than 24 hours and 2% when spasm was not present. Athavale (1974) have reported 50.4% mortality when period of onset was less than 24 hours and 1% when even the mildest spasm was not present.

In the present study it was observed that mortality increased with increasing grades of severity of tetanus on admission. This was in accordance with the Patel and Joog's system of grading tetanus severity. In the tetanus neonatorum mortality was 25%, 38.46%, 68.42%, 87.36% and 87.62% from grade I to V respectively. Athavale et al (1974) have reported neonatal mortality as 0, 18.1%, 30.8%, 61.4% and 96.8% from grade I to V tetanus cases respectively. In our study in childhood tetanus cases mortality was 0, 11.47%, 29.88%, 35.44% and 51.85% from grade I to V respectively. Athavale (1974) have reported mortality as 0.6%, 5.5%, 26.5%, 35.7% and 55.9% from grade I to V tetanus respectively. Chugh and Sehgal (1980) have reported neonatal mortality as 0%, 20%, 60%, 61.9% and 87% in grade I to V tetanus cases respectively.

It was observed in the present study that shorter the duration of symptoms were before admission, higher was the mortality. Mortality was 73.42% when duration of symptoms on admission was 1 day. Athavale et al (1974) and Phatak et al (1973) have also reported higher mortality with short duration of symptoms before

admission. The longer duration of symptoms before admission indicates slower evaluation of the disease with milder manifestation (Athavale et al, 1974).

In our study most tetanus deaths occurred within the first week of admission in hospital. The maximum deaths occurring on the first and second days following admission (41.25% and 22.61% respectively). Vaishnava et al (1966) have reported similar observa tion. In our study maximum neonatal deaths occurred on first day (57.1%). Athavale et al (1974) have reported 58.9% neonatal deaths occurring on 1st day of admission. In out study maximum childhood deaths occurred(36.36%) on 1st day of admission and 29.87%) on 2nd day. Athavale et al (1974) have reported 62% deaths within 2 days of hospital admission. In our study maximum adult tetanus deaths occurred within 2 days of hospital admission. Similar findings have been reported by Jolly et al(1974).

THERAPY

Due to the availability of human antitetanus immunoglobulins the treatment of tetanus has become safer as compared to past and even in the present time with the use of antitetanus serum (ATS) of equine origin. The present study was conducted to assess the efficacy of human antitetanus immunoglobulins(TIG) in tetanus especially when administered by intrathecal route.

In the present study human antitetanus immunoglobulins proved more effective as compared to ATS in controlling the tetanus. Vaishnava et al (1966) have reported that antitetanus serum has little value in the treatment of clinical tetanus. Florey and Fildes(1927) have reported that intrathecal use of antitetanus serum has no role in improving the survival of tetanus cases. Bhandari et al (1980) have also reported that intrathecal use of ATS has no role in improving the survival. F.W. Andrews (1917) have reported that intrathecal antitoxin of horse serum provoked inflammatory changes in the meninges.

In the present study it was observed that human immunoglobulins were more effective in the treatment of tetanus as compared to ATS in all the grades of tetanus in all the age groups. It was observed that human antitetanus immunoglobulins were more effective when administered by intrathecal route in all the grades of tetanus and in all the age groups when compared with intramuscular TIG.

Beneficial effects of intrathecal route have been reported by Ilidrim (1974 and 1969). In our study neonatal mortality decreased with the use of intrathecal TIG as compared to intramuscular TIG. Over all neonatal mortality was 72.1% with 0% in grade I and II, 20% in grade III, 75% in grade IV and 83.1% in grade V. Chugh

and Sehgal (1985) have reported 74.3% mortality in tetanus neonatorum by the use of intrathecal TIG. Chugh (1980) and Sehgal (1980) have reported that administration of human TIG via intrathecal route did not change the prognosis even in milder cases of neonatal tetanus. When compared with intramuscular human TIG. In our study neonatal mortality with the use of intramuscular human TIG was 85.71% with 0, 50%, 80%, 90%, and 100% in grade I to V respectively. Thus in our s tudy there was significant difference in the mortality in milder cases of tetanus neonatorum in both the groups. Neequaye and Nkrumab (1983) have reported no significant difference in the survival in mild to moderate cases of neonatorum tetanus receiving human TIG via intrathecal route when compared with intramuscular route.

In our study mortality in childhood tetanus cases was 20% when human TIG was administered via intrathecal route as compared to intramuscular route as compared to intramuscular route 26.6% and ATS 43.83%. Thus there was a significant differences in survival by the use of human TIG as compared to ATS. With the use of intrathecal TIG mortality was zero, 11.11%, 26.3%, 38.1% from grade I to V respectively as compared to intramuscular route where mortality was 0, 12.30%, 33.33% and 75% from grade I to IV respectively. No

patient received intramuscular TIG in grade V. In adult tetanus cases mortality was 36.1% with the use of intrathecal human TIG as compared to 62.3% with intramuscular TIG and 66.7% with use of ATS.

Sanders et al (1977), Kaswani et al (1980) Gupta et al (1980) and Diopmar et al as quoted by Habermann (1978) have reported beneficial effects from intrathecal human TIG when compared with ATS in non neonatal (Children + adults) tetanus cases. Vakil et al (1979) have reported no beneficial effect of intrathecal human TIG/ATS. It was seen that intrathecal TIG was more effective in milder cases of tetanus. Gupta et al (1980) also found similar observations with intrathecal TIG. In their series tetanus mortality was reduced significantly with intrathecal TIG as compared to intramuscular TIG in patients with mild tetanus when administered early in the disease.

In our study intrathecal human TIG was effective in all the grades of tetanus although its efficacy decreased with increasing severity. Tetanus toxins once bound to its neuroreceptors retains the ability to fix with and be neutralized by antitoxin without being split from receptor. The efficacy of intrathecal TIG can be explained on this basis. Intramuscular human TIG was not as effective probably it fails to reach the CNS quickly in the required concentration (Gupta et al,1980).

In our study it was observed that higher doses of human TIG were more effective in lowering the tetanus mortality. The mortality was 64% with a dose of 250 I.U. TIG, 43.70% with a dose of 500 I.U. TIG and 31.03% with a dose of 1000 I.U. or more doses of TIG. Thus it can be concluded that the doses of TIG between 500 to 1000 I.U. should be administered by intrathecal route to achieve its beneficial effect in tetanus cases. Chopra et al (1986) also found beneficial e ffect of intrathecal TIG in high doses in moderate and severe cases of tetanus. On the contrary Vakil et al (1977) found to beneficial effect of increasing doses of TIG.

In our study mortality was lower in all the grades of tetanus cases when human TIG was administered on the day of admission. Mortality was 100% when TIG was administered on beyond 3rd day of admission. This proves that in order to be effective, TIG should be given as early as possible after admission in hospital. Keswani et al (1980) have reported that with intrathecal administration of ATS within 24 hours. There was a mortality of 21.05% which increases gradually with delay in administration of ATS. Sanders et al (1977) postulated that free toxin is available for neutralization by intrathecal administration of tetanus antitoxin which cannot cross the blood brain barrier. But probably

after 48 hours when the toxin is presumed to be fixed to the nervous tissue intrathecal antitoxin is not of much value. Better survival by the use of human TIG via intrathecal route can be explained by the fact that when given systemically the large molecules cannot cross the blood brain barrier and so cannot neutralise the unfixed toxins already present in C.N.S. (Ildrim et al, 1969).

The intrathecal instillation of TIG needs to be performed with care due to the risk of tonsiller herniation as the C.S.F. tension is raised in tetanus but no complication was noted in our study due to instillation of TIG by intrathecal route. Human tetanus immunoglobulins were found to be safe, free from any side effects and much effective than other specific treatment available till now for the treatment of tetanus.

C O N C L U S I O N

CONCLUSIONS

The following conclusions were drawn from the undertaken study :

1. Tetanus is widely prevalent in the Bundelkhand region. It comprised about 1.01% of total hospital admission.
2. Tetanus deaths constitute about 7.54% of total hospital deaths.
3. The occurrence of the disease is more common in male in all the age groups (M : F = 1.4 : 1).
4. Tetanus predominantly occurs in rural areas. There was a lower incidence and higher mortality in the urban areas. Rural areas contributed to a higher incidence and a lower mortality.
5. Nearly half of the tetanus cases occurred during the rainy season (July to October).
6. About one third of the total tetanus cases were neonates (29.22%), adults contributed 37.53% of total tetanus cases whereas children contributed to 39.25% of total tetanus cases.
7. The mortality from tetanus was highest among neonates (82.84%) and lowest in children (28.30%) Adults had a mortality of 50.16% due to tetanus. Thus tetanus is less fatal in children.

8. Besides injury, otitis media in children, puerperal sepsis and abortion in adult females were the chief aetiological factors of tetanus.
9. Overall case fatality rate due to tetanus was 52.44%.
10. In tetanus neonatorum the mortality was higher with a lesser age of the patient.
11. Most of the neonates were delivered by local untrained dais or elderly lady of the house and shaving blade was commonly used for cutting the cord.
12. The tetanus mortality increased with increasing grades of severity of tetanus.
13. Among adult, patients, post partum tetanus had the highest fatality rate (65.78%), fatality was also high in old patients.
14. The shorter the incubation period, worse was the prognosis of tetanus patients. Mortality was 73.76% with incubation period of less than 7 days, and 15.94% with incubation period of more than 21 days.
15. The shorter the period of onset, worse was the prognosis, where the period of onset was less than 24 hours, mortality was 81.32%. Mortality was lowest (5.67%) in absence of spasms.

16. The initial 48 hours following hospital admission of tetanus cases are very crucial as the effective management can reduce mortality to a great extent.

17. Human antitetanus immunoglobulin(TIG) was only effective when administered as early as possible during the course of the illness. It was useless if administered on or beyond third day of admission.

18. In tetanus therapy intrathecal administration of TIG was superior to the intramuscular route in all the age groups and in all the grades of severity of tetanus.

19. Higher doses of human TIG were more effective in lowering the mortality. The doses of human TIG of 1000 IU or more were more effective than 250 IU and 500 IU of human TIG.

20. Respiratory spasms leading to severe apnoea was the most important cause of death in tetanus. Secondary lung infection topped the list of complications in tetanus patients.

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